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THE ATOM AND HUMANITY[1]

By Professor HAROLD C. UREY

UNIVERSITY OF CHICAGO

ALFRED NOBEL, whose birthday we celebrate to-day, was the inventor of dynamite and of smokeless propellant powders. At the same time that he engaged in this scientific research he was very much interested in bringing lasting peace to the world. In a conversation with his friends he remarked that his explosives would bring peace more quickly than peace societies. After some fifty years we now realize that Nobel was wrong in his conclusion, and we find that the peace societies were also unsuccessful.

To-day we are faced with far more powerful explosives than any that Nobel dreamed of, and we are still discussing wars and means of bringing peace to this planet. It is my purpose to discuss the relationship of this newest weapon, the atomic bomb, to the problem of world peace. May I say that this discussion has no relationship to any atomic bomb legislation or any diplomatic moves of the United States Government. It is intended to bring the urgency of the problem before you and to discuss some long-time views relative to enduring peace.

First of all I wish to show that the progress of every weapon that has been invented by man proceeds through the stages of crude invention to successful improvements, and the development of counter measures against it. The position of weapons of this kind as we know them to-day, is that they are in use by major combatants; that they produce a great deal of destruction in modern war, and that no completely decisive defense against them has ever been secured.

[1] Address delivered at the luncheon commemorating the birthday of Alfred Nobel, on October 21, 1945.

Only when a weapon is completely superseded by a more effective one does it disappear from war. Following this line of argument we may expect that our atomic bombs will be obsolete only when more terrible weapons have been developed.

Machine guns were invented in the seventeenth century. They were relatively ineffective until the first world war, when they were firing 600 or 700 rounds per minute, and accounted for many casualties. During the second world war machine guns of many varieties were mounted on planes, tanks, ships and other mobile mounts. Fighter planes carried as many as eight machine guns, and the large bombers were fully armed to take care of attack from any direction. The principle has been applied to larger caliber weapons, and these have had automatic aiming devices of great efficiency attached to them. No decisive counter defense against the machine gun has been found, and there is no indication that any government in the world thinks that it does not need machine guns in modern war.

A submarine sunk the *Housatonic* at Charleston during our Civil War. Submarines were steadily improved. In the 1890's they had reached a size of about 200 tons. In the first world war they began with 600–800 tons and rose in size to about 2,000 tons. In this last world war they very nearly won the battle of the Atlantic. Many counter measures against the submarines were devised, and were found to be more expensive than the submarines which they fought. We won the battle of the Atlantic, and the submarine was temporarily out. At the present time the talk is of larger submarines, and it is believed that they can be built.

The airplane was developed in the first years of this century. During the first world war it was used for scouting, and before the end of the war carried a machine gun. At the beginning of World War II the plane had evolved into the complicated machine of metal with engines of high power using high-grade gasolines as fuels and carrying many machine guns and modern size bombs. Before the end of the war they evolved into enormous machines carrying many tons of bombs and machine guns to defend them. They finally were powered with jet-propelled engines and carried rockets to attack other airplanes and other objectives.

They destroyed the cities of Germany and Japan and damaged cities of England, Russia, China and Poland. No decisive defense against the airplane is known. Many intercepting devices have been developed, and they do prevent the plane from exerting its full effect. Only superior air power was effective. Each combatant threw in every ounce of effort to manufacture more and better planes, bigger and more numerous bombs and more clever mechanisms to guide them and to detect them. And the victory came to the combatant with the greater industrial capacity.

This victory came only after all combatants, with the exception of the United States, had been very seriously damaged by this weapon of modern war. In the future we may expect larger and faster military planes, and all cities of the world can be expected to crumble under the loads of ordinary bombs which such planes will carry. Some will be intercepted, but some will get through any defenses that we are likely to devise.

I could repeat this story with tanks, plane carriers, high caliber guns and many other weapons great and small. Any abolition of a weapon is due to the invention of something still more effective in destructive power.

We might further mention some new weapons which were developed in this war. The V-1 or the so-called buzz bomb caused some damage, but was rather easily intercepted because of its low speed. The V-2 was in a very different category. At the beginning of the war rockets were essentially toys, but at the end of the war this rocket traveled 200 miles and rose nearly 100 miles above the earth and arrived at a velocity above that of sound so that it could not be heard before it arrived. It seems that this weapon can be further improved and probably can be aimed from still greater distances and guided by radio. It can be expected that it will follow the same course as others which we know.

Finally there is the most spectacular weapon of all —namely, the atomic bomb. This weapon stopped the war and probably saved the lives of many allied soldiers. It also presents the people of the world with a most momentous problem. Briefly, it destroyed two cities of Japan. Four square miles of Hiroshima were utterly destroyed, and the area of devastation in the case of Nagasaki was even greater —approximately 10 square miles. The total area of the city was not destroyed because of its narrow shape. The energy liberated was approximately equivalent to that released in the explosion of 20,000 tons of TNT. These two bombs were the second and third of this type to be exploded, and the third one was definitely an improvement on the second.

In regard to the future development of this weapon, we can confidently expect that it will follow the course of other military weapons which I have discussed briefly above. We can hardly think that the atomic bomb is as primitive as the early machine guns, submarines and airplanes, at this stage, but that great improvements are possible seems a certainty. One can be quite sure that the ingenuity of man will make possible the manufacture of such bombs on a large scale.

Due to secrecy maintained in the development of

this bomb, the attacks on the Japanese cities came as a complete surprise to the enemy. A single plane carried each bomb over its target. No attempt at interception by the enemy was encountered, so that bombing conditions were favorable as compared with what they would have been had the enemy expected such an attack.

The light construction of Japanese cities undoubtedly contributed to the vast destruction effected. It is hardly to be expected that steel structures would crumble so easily, though photographs of some of the industrial plants showed masses of twisted steel in the burned-out plants. In a modern city the destruction might not be so complete, but there is no doubt that the destruction would be vast and would probably set fires which would completely destroy modern buildings.

This weapon at its initial trial represents an advance over existing weapons beyond that secured by any other weapon ever devised, and considering the sort of weapons already mentioned this is indeed a remarkable statement. This weapon poses one of the most serious problems ever faced in the history of man, and beside it other problems fade into insignificance. I am amazed that any one can take our present-day strikes, reconversion, transporting the soldiers home from abroad and other current problems very seriously. They will all be solved some way, and their solution, whatever it may be, will not affect any of us very greatly. But atomic bombs are a different matter entirely.

Let us consider the problem of a war of atomic bombs. X years from now we shall have a stock pile of these weapons and will have unprecedented power in our hands. If only no other countries have them we shall feel very safe and secure. Of course, the citizens of any other country in the world will feel the same way. Thus the British will feel safe if Britain has these bombs and no other country has them; the Russians will feel safe if they have them and no other country does, and so with the people of other countries, but if all the countries of the world have them none of us will feel safe; on the contrary, we shall live in constant fear of sudden and violent death. A world of vast fear and apprehension will be our lot and that of our children. Whereas Hitler thought he could win his war in months, these weapons will encourage future aggressors to attempt the conquest of the world in a few days.

I have already mentioned what we may expect in regard to the future development of bombs based upon the past experience with military weapons. It is unnecessary for me or you to have any special information in regard to future plans for atomic bombs to draw this conclusion. But even if no improvement in the bomb were possible, what we have learned from the newspaper accounts of the bombs already exploded, shows that they are bad enough. If one bomb will devastate an area of 10 square miles 1,000 bombs of this kind if properly placed would devastate 1,000 square miles. The area of New York City covers a densely populated area of about 300 square miles. From this it is easy to calculate that these 1,000 bombs if properly placed would destroy thirty-three cities of the size of New York.

And what is there to prevent our assuming that with sufficient effort 10,000 bombs can not be secured? It is wrong to assume that these weapons can not be made in large numbers as a result of future improvements in known processes.

During World War I, a strip of country across northern France and Belgium was laid waste. In World War II the cities of Germany and Japan were almost totally destroyed, as were some of those of Russia and Poland. Extensive damage was done to the cities of England. Without considering the contribution that atomic bombs may make to the destruction of cities in future wars, is it not reasonable to expect that much more damage will be done in World War III? Is it not probable that the cities in the United States would also suffer?

If atomic bombs are used in the next war it seems certain that all the principal cities of the world, including those of the United States, will be utterly destroyed and their inhabitants killed. Perhaps some will disagree with this statement, but perhaps we can settle on half of them being destroyed, or a third, but does this make any difference in our considerations. Let us accept the fact that an atomic bomb war is bound to be much more destructive than this last war; that it is bound to extend to all the industrial countries of the world.

We can expect that counter measures will be devised, just as they have been in other cases. Some of these counter measures will interfere with the delivery of the bombs. We can also expect that counter measures to the counter measures will be developed, and more effective methods for the delivery of bombs will be devised. It may be possible to interfere with the delivery of the bombs, but then some new device will be found by some one which will then make their delivery possible. What I wish to say is that we can not expect that a defense so effective that either the United States or any other country will decide that it is useless to manufacture such bombs will be devised. It will again be the case of dog eat dog, and much effective indiscriminate biting will result in the process. Let us then set aside the assumption that a decisive defense will be secured. Such an assumption would be contrary to experience and would be the most foolish of wishful thinking.

But we may ask whether other countries will get

these weapons. It seems unnecessary to answer this question. What weapon ever devised by man ever remained the possession of the country of origin? Did this apply to machine guns or submarines or planes or tanks or high explosives or gas or guns of any kind? We may rest assured that other countries can secure atomic bombs and may secure them more quickly than we think.

Many people ask how long may it take other countries to secure these bombs, and various estimates have been made. General Leslie R. Groves has estimated that this will be from 5–10 years. It took us 3½ years from the start of serious efforts to the time when the first bomb was exploded. Further time is needed for production of an adequate supply for a really full-scale war. We should note that the British start with nearly full knowledge of our processes, and the whole world knows our lines of attack on the problem, and that these lines led to success. This is a very great advantage. Other countries at the present time must be very much afraid of the United States, in spite of the fact that aggressive war or any kind of war is far from the minds of the people of this country. The scientists, engineers and citizens of other countries will feel that their respective countries are in dire peril.

Just imagine our sense of fear were some other country in possession of atomic bomb plants and we were not. This sense of emergency will call forth the greatest effort on the part of other countries, and I think the lowest figure given by General Groves is the safer one for these considerations. Let us then assume that we have five years in which no other country could attack us with atomic bombs.

What shall we do under this threat in this brief respite? This is a very difficult question because the problem is a very complex one. Incidentally, the problem is not made different nor more complex by the atomic bomb, for the destruction that could be made without its aid would also present a very serious problem to the world. The atomic bomb really accentuates the difficulty, and perhaps is of real value to us in bringing forcibly to our attention the grave problem ahead of us, and it may induce us to make concessions from our established ways of thinking which are necessary if destruction by this means is to be avoided.

In a democracy it is necessary to have an informed people if proper decisions are to be made and executed. We must all understand that the most devastating weapon of all times is now in our hands and will soon be in the hands of other industrialized countries. We should face the facts and not engage in wishful thinking, for wishing will never remove the threat of this bomb. We should rise to our responsibilities and not merely put the matter aside because we wish so much to get back to our peace-time pursuits.

We can not pass this on to the Congress or to the President, for they can not act effectively without the approval of the people of the United States. Also, they should not move contrary to the wishes of the citizens of this country. We must first understand the magnitude of this problem and then must be prepared to act with courage.

Let us consider some possible ways of controlling the atomic bomb. In the first place, many people suggest that we should make ourselves stronger than all other nations. This is implied in all the discussion of keeping the so-called "secret" of the bomb. In my opinion if we published all our data in detail we would not shorten the five or ten years of General Groves's estimate by very much. It takes time to build plants, and it takes time to operate them.

The whole question of the atomic bomb secret is not important in itself. What is important is the policy back of it. Do we intend to engage in an armament race with other countries of the world? If the answer is yes, we should try to inspire all our people to go to work on this problem in order to produce the greatest number of the biggest bombs that can be devised, and to devise the most effective way of delivering them to those enemies of the United States that we intend to attack or that we fear will attack us. This policy will result in an atomic bomb war with all the destruction that I have tried to emphasize in this talk, and this is exactly what I should like to see avoided.

We may try to outlaw the atomic bombs in the future. Some people say that poison gas was not used in this war because of such agreements between sovereign nations. That is only a partial truth. It is certainly a question as to whether high explosive and incendiary bombs are not more effective, ton for ton, than is poison gas, for the former not only kill people but destroy cities, while the latter leaves the cities intact.

If atomic bombs are in the possession of potential enemies of the United States we shall all be afraid that they will be launched against us by means of rockets, pilotless planes or something else, and without warning. We must watch our borders for all stray planes that might be coming in. We must introduce a police system that will be able to detect any possible planting of these bombs in our cities where a mere alarm clock would set them off at a predetermined time. The fear and tension under which we will live will make us very nervous indeed. Every country of the world will have an itchy trigger finger if we all have the atomic bombs and merely an agreement not to use them.

I do not trust any such way of controlling the use

of atomic bombs. If the nations agree not to use them and are sincere, then they should also agree not to make them. Incidentally, the Pope tried to outlaw the cross-bow in the twelfth century and from that time to this no outlawing of weapons between sovereign states has been effective.

The suggestion is made that we turn the bombs over to the United Nations organization to enforce peace. This suggestion is better, but it also has difficulties. Where would we store the bombs in the possession of the United Nations? Europe and Asia would object to North America, and we would object to Asia or Europe. How about Africa? You can imagine that the United Nations would have an effective small policing army powered with atomic bombs at some isolated point. Would we not all be afraid of the United Nations organization? Would we not fear that some Hitler might gain control of those weapons and subjugate the world in a very short time?

There is another difficulty. We presume that if the United Nations has a store of such bombs, it proposes to use them in emergencies. Let us assume that manufacturing the bombs in any country is a criminal offense, but that in spite of this the administration of the United States decides that it will make these bombs. The United Nations can then use the bombs to interfere with this operation. They will use them to destroy all the manufacturing facilities that might be set up. In so doing they will kill a very large number of quite innocent people, and the effect will be to unite the entire country against the United Nations.

If one wishes to police any state or nation, or the world, one wants to use weapons for the police purpose that will distinguish between those who violate a law and those who do not. If one can do this the law-abiding citizens will aid you against the law breaker, but the use of a large weapon of necessity unites all classes against the policing power. Atomic bombs are good for nothing but wars and for the destruction of large cities and their populations and large industrial plants.

But this proposal to turn the bombs over to the United Nations leads to a further suggestion. If we turn over the most powerful weapon to the United Nations why not also turn over all large caliber weapons of all other kinds for, of course, they are relatively ineffective against a superior weapon. And then we come to the next step. If we have turned all our large caliber weapons over to the United Nations, it is unnecessary for this organization to have them either, for there is no one to oppose them.

We are inevitably led to the conclusion that a superior world government of some kind possessing adequate power to maintain the peace and with the various divisions of the world relatively disarmed, is the only way out. What will be needed is a most efficient inspection service which will detect and report promptly any attempt to produce atomic bombs or other heavy arms and a sufficient police force to prevent such activities. In this way neither the countries of the world nor the United Nations organization will have atomic bombs and no one will need to fear them.

I am not so naive as to think that this is a solution easily arrived at. I am not even so sanguine as to think that there is a high probability that logical action of this kind can be accomplished without the dubious advantage of a third world war. But I pass the problem to you now. Do you see any way to avoid the threat of an atomic war?

I think I have said enough to give my audience an opportunity to think these things over. I trust the conclusions of an informed populace of the United States. I believe that the considered judgment of the whole people is a reliable guide, and, after all, it is the people of the United States who face destruction and death, and they should have the privilege of making their own decisions.

There are a number of statements which I would categorically defend, and I wish to present them to you:

(1) If atomic bombs are made in one country they will be made in all industrial countries of the world.

(2) If atomic bombs are made in all these countries we will spend all our days in deadly fear that they will be used, and in time they undoubtedly will be.

(3) By one means or another no atomic bombs must be made anywhere in the world and they must not be in the possession of any government of any kind.

(4) The peace-time applications of atomic energy, or, in fact, of anything else, are of no importance whatever unless the danger of atomic bombs is banished from the earth.

In conclusion, may I repeat the hope of Alfred Nobel, that this weapon is sufficiently terrible to make possible the bringing of peace to the earth.

OBITUARY

ACADEMICIAN V. I. VERNADSKY
1863–1945

THE news came from Moscow of the death on January 6, 1945, of Professor V. I. Vernadsky (see SCIENCE, 101: 110, 1945). With his passing Russia lost one of its oldest and most distinguished scientists of international renown.

Vladimir Ivanovich Vernadsky was born on March

13, 1863, a son of a professor of Moscow University, and educated first in that city and later at St. Petersburg University, from which he was graduated in 1886. He was appointed a docent of mineralogy of Moscow University in 1890 and received his master's degree in 1891. In 1897 he was awarded a Ph.D. degree for his thesis, "The Phenomena of Gliding Planes in Crystalline Substances." He soon won fame for his classical research on silicates. One of his most important works on that subject is: *"Sur le groupe de la sillimanite et le rôle de l'alumine dans les silicates"* (1892).

Being a brilliant lecturer and educator he reformed the teaching of mineralogy in Moscow University and was practically the founder of chemical mineralogy based on historical methods. Outstanding Russian mineralogists, such as the late V. Archangelsky and A. Fersman, were students of Vernadsky. His widely known voluminous "Essay on Descriptive Mineralogy" (1908) is a standard work on mineralogy in Russia.

In 1906 he was elected a member of the Academy of Sciences. Since that time, he turned his attention to geochemistry and study of the isomorphism of chemical elements. In 1915 he took a leading part in the organization of the Commission for the Study of Natural Resources of Russia, from which a number of scientific institutes later emerged. Vernadsky was made in 1922 the head of the Radium Institute and engaged energetically in study of the role of the radioactive elements in the history of the development of our planet. He was first to introduce the method of the determination of the age of rocks and minerals by the rate of their radioactivity and he made great contributions in that field of science.

He was also very interested in the problem of the role of micro-organisms in the biogeochemical processes in the earth's crust, and for the purpose of its solution, he founded in 1918 the Biogeochemical Laboratory of the Academy of Sciences and was its director since 1920 until his death.

The last period of Vernadsky's activity was devoted mostly to the study of geochemistry. His classical work "Ocherki geokhimii" ("Essays on Geochemistry") sustained four editions and was translated into French, German, Japanese, etc.

This in no way exhausts the list of the activities of Professor Vernadsky. We can mention only briefly his attainments in other fields of science: the study of physical and morphological properties of meteorites, the organization and development of balneologic centers and the founding of the Ukrainian Academy of Sciences, of which he was president in 1918, etc.

He visited Europe many times and was very well known in European scientific circles. His outstanding work was recognized by both the Imperial and Soviet governments and by the science world and he was the recipient of many honors and distinctions. In 1942 he was awarded the full prize of 200.000 roubles for his research in geochemistry and genetical mineralogy.

His colleagues in the Academy of Sciences and in Moscow University mourn him not only as a famous scientist but as a noble, simple and good-natured man and as a faithful friend.

VLADIMIR C. ASMOUS

ARNOLD ARBORETUM,
HARVARD UNIVERSITY

DEATHS AND MEMORIALS

THOMAS J. MANEY, research professor of pomology in the Iowa Agricultural Experiment Station, died on October 12 at the age of fifty-seven years.

DR. HENRY B. KUMMEL, from 1902 to 1937 state geologist of New Jersey, died on October 23 at the age of seventy-eight years.

DR. JAMES H. BEAL, senior past president of the American Pharmaceutical Association, Remington medalist, died on September 20 at the age of eighty-four years.

DR. E. J. WILLIAMS, F.R.S., professor of physics at University College, Aberystwyth, Wales, died on September 29 at the age of forty-two years.

DR. PAUL RUGGLI-BLUME, professor of chemistry at the University of Basel, died on September 4 at the age of sixty-one years.

ON the opening of the fall session of the Medical Branch of the University of Texas at Galveston, the auditorium of the out-patient clinic building was named Randall Hall in honor of Dr. Edward Randall (1860–1944), who served as professor of materia medica and therapeutics from 1890 to 1929, when he became professor emeritus and chairman of the Board of Regents of the university.

A MEMORIAL meeting in honor of the late Professor Pio del Rio Hortega was held on October 31 by the Montreal Neurological Institute. The speakers were Dr. Wilder Penfield, Dr. Pierre Masson, Dr. Miguel Prados and S/L William Gibson.

SCIENTIFIC EVENTS

THE ARMY MEDICAL RESEARCH AND DEVELOPMENT BOARD

A BOARD to be known as the Army Medical Research and Development Board has been constituted in the Office of the Surgeon General. It will be responsible for the planning and general supervision of all Medical Department research and development activities. The membership will include the chiefs of the various

professional services and divisions of the Office of the Surgeon General; the air surgeon; the ground surgeon; the chairman of the Division of Medical Sciences of the National Research Council (by invitation); and the chairman of the Committee on Medical Research, Office of Scientific Research and Development (by invitation). The board has two operating divisions, the Research Division and the Development Division, to carry out its plans. It is the intent of the Surgeon General to carry on an active program of research and development during the postwar period and the new board should provide the means for maximum coordination of effort within the military service and cooperation with civilian and Federal research agencies. The immediate tasks facing the board are three in number. Essential research must be continued in the existing research and development laboratories of the Medical Department in spite of the personnel difficulties of the period of demobilization. Plans must be made and implemented for the continuation or actual expansion of research and development in the postwar period. The demobilization of the Office of Scientific Research and Development necessitated finding other sponsorship for those research contracts of the Committee on Medical Research which warrant continuation even though hostilities have terminated. A group of these contracts will be taken over by the Medical Department and administered by the board.

THE MOUNT PALOMAR TELESCOPE

CONSTRUCTION of the world's largest telescope—(200-inches) at the summit of Mount Palomar in California—is being resumed after a wartime interruption. Between one and two years will be required for its completion according to an announcement made by the Carnegie Institution of Washington, which cooperated with the California Institute of Technology in the design and operational plans. The uncompleted reflecting telescope is now at the observatory on Mount Palomar, sixty-six miles north of San Diego.

The 200-inch glass disc was poured on December 2, 1934, at Corning, N. Y., and was taken across the country to be placed in the observatory. With the outbreak of war both the optical and mechanical work had to be suspended.

Plans have been formulated by the Carnegie Institution, which operates Mount Wilson Observatory in California, for a cooperative research program between Mount Wilson and the Mount Palomar Observatory as soon as the equipment at the latter is completed. According to the announcement both institutions have approved a program whereby "the two observatories will be placed under a single administrative management, having a director who will be chairman of an advisory management committee with representatives from both organizations."

THE ATOMIC ENERGY ACT

AN appeal for more complete consideration of the Atomic Energy Act, signed by one hundred and fifty-five scientists of the Boston area, was telegraphed to President Truman on the morning of October 23. Those signing the telegram—including Dr. Karl T. Compton, president of the Massachusetts Institute of Technology, and Dr. Leonard Carmichael, president of Tufts College—are members of the National Society of the Sigma Xi. The need for resumption of hearings on the bill is emphasized. The telegram follows:

The undersigned scientists of the Boston area, members of The National Scientific Research Society, feel deep concern over the very brief and inadequate discussion of the Atomic Energy Act of 1945. Widespread fears have been expressed regarding the sweeping nature of the powers delegated to the Atomic Energy Commission in the proposed bill, and without attempting to take a stand on this point, we feel it is imperative to give the fullest opportunity for discussion on this and other points both in Congress and by the public at large. Whatever the urgency of such legislation, the need for full and complete understanding of the momentous issues at stake is much greater. We urge strongly that hearings on the bill be resumed and that the fullest public consideration of the question be encouraged.

Copies of the telegram have been sent to John W. Snyder, director of War Mobilization and Reconversion; Representative Andrew J. May, chairman of the House Military Affairs Committee, sponsor of the bill; Representative Chet Holafield, member of the House Military Affairs Committee, and John W. McCormick, House of Representatives. Those signing the telegram from Harvard University included Professor Harlow Shapley, director of the Observatory; Dr. Lionel S. Marks, Gordon McKay professor of mechanical engineering, emeritus; Dr. Percy W. Bridgman, Hollis professor of mathematics and natural philosophy; Dr. John H. Van Vleck, professor of mathematical physics; Dr. Jabez C. Street, associate professor of physics, and Dr. Kirtley F. Mather, professor of geology.

NEWS FROM ABROAD

THE following is a translation of a letter from Professor J. Timmermans, president of the Bureau of Physico-chemical Standards, International Union of Chemistry; University of Brussels, Belgium, addressed to Dr. Marston T. Bogert, as president of the International Union of Chemistry:

August 29, 1945

Dear Colleague:

As Professor Dony-Henault will already have told you,

we are occupied in resurrecting our National Committee of Chemistry, decimated by the war, and I hope that it will be functioning again before the close of this year.

Meanwhile, permit me in a personal way to direct your attention to a question presenting great interest for all chemists and where your intervention as President of the Union appears to me distinctly desirable.

The matter is the following: On returning* to Brussels, I found in our university laboratory library the new volumes of Gmelin-Kraut and of the second supplement of Beilstein, which appeared five years ago. These works are of such value for chemists of the entire world that it seems to me necessary to undertake as soon as possible (if not already too late) conservation measures to assure their continuation. Without attempting to predict the future, one can perfectly well conceive that the publication might be continued outside of Germany. There might be a chance, it seems to me, to save all that remains of the documentation collected in the Hofmann House at Berlin on the subject, as well as MSS in preparation, and eventually to assure the gathering of certain members of the specialized personnel who prepared these works. Could you not take up this question with the authorities of the American army of occupation in Berlin? Such is my wish and the purpose of this letter.

Please accept, my dear President, the assurances of my best regards.

(signed) J. TIMMERMANS.

Dr. and Mrs. Blakeslee have received the following letter, under date of September 6, from Dr. Otto Lous Mohr, of the Institute of Anatomy of the University of Oslo:

Sincere thanks for your kind card (of May 27). It was a great joy to hear from you—as a matter of fact it was one of the very first greetings we received after all these years of complete isolation.

Happily, we are all well, but it has been a terrible time. Mrs. Mohr was the first of us to be arrested, but that was in the spring of 1941 when conditions were not yet as bad as later on. And she was released the following day. I myself was imprisoned Sept. 1941 during an "Ausnahmezustand" together with our university rector and two other professors. It was the day after the first two Norwegian civilians had been shot by the Gestapo, and if the students had not kept quiet we would probably have been shot too. After 7 months in jail and concentration camps I was released but strictly forbidden to live in or near Oslo and not to speak of entering the University. So when I was now again appointed professor, May 1945, I had not been at the institute for 4 years. October, 1943 our son was arrested, brought in a concentration camp and somewhat later sent to Germany (Elsass, Buchenwald, Neuengamme) with two other Norwegian students. It is a mere wonder that he—thanks to the Bernadotte action—returned safely late in May after our liberation. In addition one of my sisters spent 2½ years in a concentration camp and my youngest brother 1 year in prison. You may from this very concentrated outline realize what the victory and liberation meant to us. We and all Norwegians can not express our profound gratefulness to the decisive part played by the Americans in this tremendous fight for liberty and decency!

Conditions out here are now gradually improving. Our University is luckily undamaged. I myself started teaching again August 1. Demerec has asked me to send him a brief record on our genetics laboratory to appear in D. I. S. so I am not going to enter upon that chapter here. We have of course considerable difficulties, but we are hopeful and eager to apply ourselves to the tasks that lie before us. Mrs. Mohr has been marvellous during all these ordeals, attended to her practice and kept things together in Oslo during my absence. She has now also regained her sleep—her nights were not good when we had our boy in Germany, neither were mine.

To live under terror for years is something not to be explained. Can you understand how so *many* people can be so utterly depraved and beastly? It is certainly not easy to believe in the progress of humanity.

Best greetings from all of us and renewed thanks for your card.

The following communication from D. Hille Ris Lambers, of Bilthoven, Holland, dated May 12, has been received by Professor E. O. Essig, of the University of California at Berkeley:

This is to inform you that I still live and still work on aphids. All during the German occupation I have worked on my books on European aphids, but nothing could be published because the Jerries did not like papers in English and they did not like me. In 1940 they caught me and put me in prison, but I was rather soon out of it. Several times my house was searched but without result. Then, this winter they ordered the whole population out of Wageningen and the neighboring village of Bennekom, and that was the worst blow because they pillaged to such an extent that we have not even beds or chairs left. All our clothes and shoes, crockery, in short everything disappeared eastwards or was wrecked. I had hidden my library and slides under the floors, but they tore these open and flooded the works. Everything which is not stolen is more or less completely destroyed by water. About 60% of the slides can be recovered but of the books a very great part is irreparably gone. I had buried my manuscripts and drawings in a steel box, but they found it and all the drawings are gone, but the box with the manuscripts in it was thrown in the garden where I found it. Fortunately, the lid had closed and so, seven months later, I found my manuscripts, about 2,000 pages both undamaged. My microscope still exists. I put it in a strong box of some acquaintance and that strong box is the only one in the area which was not opened. But I have no means to make new slides because the 20 boxes of coverslips were stolen as well and even the doctors have no coverslips in this totally exhausted country.

My house got a full hit from an Allied 25-pounder which exploded just beside my working desk. About 100 yards from it a German V-I exploded, so that the house

* From his refuge in England.—M.T.B.

is cracked and the tiles are mostly gone. All the windows are out too, but I have two panes now so that we will have light in two rooms if within a few weeks we go back. Friends and family gave us some beds, chairs, a table, cups, plates and a few others of the most essential things for living. You can buy nothing except food on coupons. All the shops are absolutely and completely empty. For weeks I have tried to get a tie, on coupons, but without any results. I wear a dyed Allied uniform, discarded boots and a shirt from the U. S. Army, which, fortunately, I got from the Red Cross. This winter hundreds died here from starvation but we survived because of my name being rather well known in agricultural circles. Still, it was dangerous to go out for food because the Jerries pinched everybody under 50 for work in Germany and I had several narrow escapes. 65% of the Dutch Jews, about 120,000 were murdered in Germany and nearly the same number of other men and women. On top of that many thousands died of starvation and many more by bombing and shellfire. We too, had six weeks of intermittent shellfire at Bennekom, but we got more or less accustomed to it, though they shot part of a house away in which we slept upstairs for a few weeks. We were so calm then, that we went to sleep and not till next morning did anybody find out that we were hit.

Before America got in the war you promised to send me some papers and some material of aphids. You could do me a very great pleasure with whatever you can lay hands on, but I am especially in a hurry to examine if possible fresh alcoholic material of the various *Micromyzus* species from *Allium* species which you described just before the war. In England a *Micromyzus* on shallot has turned up, which is thought there to be new and for both the identification of their species and the purpose of including it in my monograph I should like, if possible, to compare it with material of your species.

The only things of interest which I published during the war were a short survey of fruit aphid in Dutch, of which I never received a reprint, but which will be reprinted eventually as a booklet, and an article on *Yesabura, Anuraphis* or whatever you want to call it, *crataegi* Theobald, from apple. The latter article is extensive and well illustrated, with an English summary, but though I got the last proof, it was not yet printed at the time of the Airborn landing near Arnheim and then the Jerries took all the better metal, but apparently the blocks still exist so that it should not be long until this is really published. Part 3 of my monograph got a permission from the Germans last summer to be printed in autumn, but after the landing all the printers' shops had to be closed. The manuscript is intact and the proofs may come in any moment. As soon as I have copies you will have them. Everything is still greatly disorganized here because so much is stolen. Everybody grows his own tobacco now but it stinks though it burns when lighted. The time that each small tobacconist sold about 200 brands of cigarettes is history now.

Well, Professor Essig, if you would please inform me how you did during the war, and if you could send me some material, you'll oblige me very much, really. My address after the middle of September will be 24, Selterskampweg, Bennekom.

With best regards and congratulations on the work your country did for us during the war and is still doing.

SCIENTIFIC NOTES AND NEWS

THE Nobel Prize for physiology and medicine has been awarded by the Karolinska Institute of Stockholm to Sir Alexander Fleming, of the University of London, the discoverer of penicillin, and two of his co-workers—Dr. Ernest Boris Chain, professor of chemical pathology at the William Dunn School of Pathology, Oxford, and Sir Howard Walter Florey, professor of pathology, also of the University of Oxford. The recipients will share equally in the prize, which amounts to about $30,000.

THE Gorgas Medal, awarded annually since 1942 for outstanding work in preventive medicine for the armed forces, was presented in Washington on October 29, at a dinner of the Association of Military Surgeons, to Captain Lowell T. Coggeshall of the Marines "for distinguished service to our military forces in establishing new principles in the management of patients suffering from psychic disturbances as well as physical deterioration from the effects of malaria and filariasis." Frank F. Law, vice-president of Wyeth Incorporated, which sponsors the medal, made the presentation of the medal and a check for $500.

THE eightieth birthday of Professor Charles Atwood Kofoid was celebrated on October 11 by the Department of Zoology of the University of California at Berkeley, by a reception in the Kofoid Library in the Life Sciences Building. Over three hundred friends and colleagues of Dr. Kofoid were invited. Many of those who were unable to be present sent congratulatory letters.

MEMBERS of the American delegation to the meeting of the Educational Conference of the United Nations, which opened on November 1 in London, include Dr. Arthur H. Compton, chancellor of Washington University, St. Louis, and Dr. Harlow Shapley, director of the Harvard College Observatory.

THE British Privy Council for Medical Research has appointed Dr. Patrick Alfred Buxton, F.R.S., professor of medical entomology in the University of London, and Sir Alexander Fleming, F.R.S., professor of bacteriology, members of the Medical Research Council.

DR. LOUIS B. SLICHTER, professor of geophysics at the Massachusetts Institute of Technology, has been

appointed professor of geophysics at the University of Wisconsin. He will take up his new work at the opening of the second semester late in January.

DR. HENRY H. BLAU, in charge of research and manufacturing of the Federal Glass Company, has been appointed professor of glass technology at the Ohio State University.

DR. JOSEPH B. SPROWLS, JR., has been appointed professor of pharmacy and head of the department at the University of Buffalo.

DR. W. F. BUCHHOLTZ, of South Dakota State College, is returning to Iowa State College as associate professor in the department of botany and as research associate professor in the section of botany and plant pathology of the Agricultural Experiment Station. Dr. Robert Dean Schick, of the University of Oklahoma, will become assistant professor in zoology in the department of zoology and entomology.

DR. JAMES O'HARA MALONEY, of the department of engineering of the E. I. du Pont de Nemours and Company, Wilmington, Del., has been appointed head of the department of chemical engineering and director of the research foundation of the University of Kansas.

DR. W. STORRS COLE has been appointed professor of geology at Cornell University.

DR. GERHARD HERZBERG, professor of physics at the University of Saskatchewan, has arrived at the Yerkes Observatory at Williams Bay, Wis. He will serve as a member of the staff of the Yerkes and McDonald Observatories and as associate professor of spectroscopy in the department of astronomy and astrophysics of the University of Chicago.

DR. R. H. K. FOSTER, chief pharmacologist with Hoffmann-LaRoche, Inc., has been appointed associate professor of pharmacology at the School of Medicine of St. Louis University.

CONRADO F. ASENJO, assistant professor of chemistry at the School of Tropical Medicine of the University of Puerto Rico under the auspices of Columbia University, has been promoted to an associate professorship.

LIEUTENANT WARREN C. WHITMAN has returned to his work at the North Dakota Experiment Station. He was attached to the Eighth Air Force in England from October, 1943, to August, 1944, and to the Ninth Air Force in France until June, 1945.

DR. D. L. BLACKSTONE has returned to the University of Missouri as assistant professor of geology after three years spent on investigations of oil and gas for the Carter Oil Company, of Tulsa, Oklahoma.

DR. RALPH MUCKENFUSS has returned to his work as director of the bureau of laboratories of the New York Department of Health, following a tour of duty as commanding officer of the First Medical General Laboratories of the European Theater of Operations. For his work in the Army he was awarded the Legion of Merit.

MAJOR ALLAN HEMINGWAY, who, prior to his entrance into the AAF School of Aviation Medicine early in 1943, was assistant professor of physiological chemistry in the Medical School of the University of Minnesota, has been placed on the inactive list of the Army and will resume teaching and research.

DR. EARL W. FLOSDORF, for twelve years assistant professor of bacteriology in the Medical School of the University of Pennsylvania, has resigned to become director of research and development for the F. J. Stokes Machine Company, Philadelphia.

DR. CHARLES A. COOK, formerly in charge of the department of medical biochemistry at the Lambert Pharmacal Company, St. Louis, has been appointed research director of the E. L. Patch Company, Boston.

DR. ROBERT D. COGHILL, since 1939 chief of the Fermentation Division, Northern Regional Laboratory, U. S. Department of Agriculture, in Peoria, Ill., has been appointed associate research director of the Abbott Laboratories, North Chicago.

DR. R. E. BUCHANAN, director of the Agricultural Experiment Station at Iowa State College, has been named chairman of the technical advisory committee of the delegation of the Iowa Development Commission to attend the first meeting of the Food and Agriculture Organization of the United Nations, which opened in Quebec on October 16, and adviser to the official delegate from the United States, Secretary of Agriculture Anderson.

PROFESSOR R. P. LINSTEAD, F.R.S., has been appointed director of the chemical research laboratory in the British Department of Scientific and Industrial Research.

DR. E. ASHWORTH UNDERWOOD, medical officer of health of West Ham, during the past five years honorary secretary of the Section of the History of Medicine of the Royal Society of Medicine, has been appointed director of the Wellcome Historical Medical Museum and the Wellcome Historical Medical Library, London. Wing Commander C. J. Hackett, a research fellow in tropical medicine of the Medical Research Council, has been appointed director of the Wellcome Museum of Medical Science in succession to Dr. S. H. Daukes, who has served for the past twenty-six years.

DR. REID B. GRAY has been appointed director of the Reynolds Research Institute, subsidiary of the

Reynolds Metals Company. He succeeds Dr. Warren J. Mead, of the Massachusetts Institute of Technology, who recently resigned.

THE Smith, Kline and French Laboratories have made a grant of $2,500 a year for two years to Professor Amedeo S. Marrazzi, head of the department of pharmacology and therapeutics of the College of Medicine of Wayne University. The grant is for the further study, by electrical methods, of drugs acting on the autonomic and central nervous systems.

DR. GEORGE HERRMANN, professor of medicine at the Medical Branch at Galveston of the University of Texas, recently spent two weeks in Mexico City as the guest of the Institute of Cardiology and of the University Medical School.

PROFESSOR JOHN R. DUNNING, of Columbia University, addressed the Faculty Science Club of Hunter College on October 16. The title of his lecture was "Nuclear Fission."

A JOINT meeting of the American Philosophical Society and the National Academy of Sciences will be held in Philadelphia on November 16 and 17. The meeting will be devoted to "Atomic Energy and Its Implications." The sessions on Friday will be held in the auditorium of the University Museum of the University of Pennsylvania, 33rd and Spruce Streets, and on Saturday at the Hall of the American Philosophical Society, Independence Square. These meetings will be open to the public.

THE American Association of Physics Teachers will hold its fifteenth annual meeting jointly with the American Physical Society at Columbia University on January 24, 25 and 26. At this meeting the fifth Richtmyer Memorial lecture will be delivered by Dr. Paul Klopsteg; presentation of the Oersted Medal will be made; joint sessions will be held with the American Physical Society, and there will be exhibits of newly developed instructional equipment.

THE New York Academy of Medicine announces the availability of the Louis Livingston Seaman Fund for the furtherance of research in bacteriology and sanitary science. One thousand dollars is available for assignment in 1945. The fund has been made possible by the terms of the will of the late Dr. Louis Livingston Seaman, and is administered by a committee of the academy under the following conditions and regulations: (1) The committee will receive applications either from institutions or individuals up to December 1. Communications should be addressed to Dr. Wilson G. Smillie, chairman of the Louis Livingston Seaman Fund, 1300 York Avenue, New York 21, New York. (2) The fund will be expended only in grants in aid for investigation or scholarships for research in bacteriology or sanitary science. The expenditures may be made for (a) the securing of technical help; (b) aid in publishing original work, and (c) purchase of necessary books or apparatus.

THE Paul-Lewis Laboratories, Inc., of Milwaukee, Wis., has established an annual award for outstanding work in the field of enzymes, and has requested the American Chemical Society to administer the award in a manner similar to other awards administered by the society. The award is to be made for the purpose of stimulating fundamental research in enzyme chemistry in the United States by young men educated in a college or university in the United States. It will consist of $1,000 and a bronze medal (or diploma). An additional amount up to $150, or as much thereof as necessary, is available to the recipient toward traveling expenses to the national meeting of the American Chemical Society at which the award will be presented. To be eligible, a nominee shall be a citizen of the United States and a graduate of a United States college or university, shall not have passed his thirty-sixth birthday on April 30 of the year of the award, and shall have accomplished outstanding research in enzyme chemistry. For the purpose of this award the presence of an enzyme action must be unequivocally demonstrated in the nominee's work. Nominations for this award, as well as members of the award committee, are limited to non-commercial chemists. J. J. Willaman, of the Eastern Regional Research Laboratory of the Department of Agriculture, has been appointed chairman of the canvassing committee.

A SUM of $500,000, from funds raised during the cancer campaign in the spring of 1945, is being made available by the American Cancer Society for initial steps in a cancer research program sponsored by Dr. C. P. Rhoads, chairman of the research committee formed by the National Research Council in cooperation with the society. Appropriations will be made for chemical, biological and clinical research, and for research in physics. The sum of $50,000 is recommended for fellowships to be given scientific men released from the Army who will engage in cancer research.

THE University of Notre Dame, South Bend, Ind., has received a gift of $1,000,000 from Peter C. Reilly, of Indianapolis, to be known as the P. C. Reilly Science Fund. Its income will be used in the field of chemistry and chemical engineering.

A SUBSTANTIAL part of the engineering library of the late Robert E. Horton, hydraulics engineer, of Voorheesville, N. Y., has been received by Albion College, Michigan, of which he was a graduate. The

bequest was accompanied by an endowment of $5,000 for the extension and maintenance of the library.

THE first issue of *Wrightia*, the botanical journal of the Southern Methodist University at Dallas, has appeared. Each volume, which will contain approximately five hundred pages, will consist of a series of numbers to be issued at irregular intervals.

As an aid in the study of legislation on science now before the Congress, the Subcommittee on War Mobilization of the Senate Military Affairs Committee has issued a select bibliography on "The Social Impact of Science." The bibliography has been prepared by the Library of Congress. It lists more than five hundred titles of books, pamphlets, articles and Congressional bills and reports dealing with the social and economic problems arising from scientific progress. A special section covers the available literature on atomic power, including several volumes yet in press.

SPECIAL ARTICLES

FORCES INVOLVED IN THE REACTION BETWEEN ANTIGEN AND ANTIBODY MOLECULES

THE nature of the reaction between antigen and antibody molecules is far from being completely understood at the present time.[1] Though of major importance from the standpoint of biology, the reaction also offers a very interesting example of the physical forces involved between large molecules. Thus for the past few years the author has been engaged in a study of the serological reactions occurring between a film of antigen deposited on a metal slide and a solution of antibodies brought in contact with that slide. From this work, which will be published shortly in detail, some surprising facts have recently come to light which appear to be of sufficient interest to justify their publication in this note.

Previously published work has shown that the specific fixation of homologous antibodies occurs even when the antigen molecule is completely unfolded and 6 to 8A thick.[2] The specific fixation of antibodies has been demonstrated by an increase in the adsorbed layer on the plate after treatment with homologous antibodies. The accuracy with which small increments in film thickness can be measured is now greatly improved by an apparatus named the "ellipsometer," recently described, which permits the measurement of film thickness increments with an accuracy of $\simeq \pm 0.3$A.[3] The method is based on the change that takes place in ellipticity of the light reflected after a metal slide has been coated with films whose thickness is of molecular dimensions. The technique employed is briefly this: Highly polished stainless steel slides are first covered with an optical gauge of 1 and 3 (or 2 and 4) layers of a reference film (stearic acid). Films of antigen (bovine albumin, egg albumin) spread on an Adam Langmuir trough are transferred on the slides according to the procedure of Blodgett and Langmuir.[4] Two unfolded films 6 to 8A thick can easily be transferred on such slides.

It is very difficult to transfer more than two layers. However, if the slide is first treated with a dilute solution of uranyl acetate, a very large number of protein films can be transferred. This demonstrates that the uranium ions strongly polarize the first layer, which in turn polarizes the second, and so on along the successive layers. This polarization prevents the films from slipping back on the surface of the trough when the slides are taken out. A drop of the antisera to be tested, diluted 1/10 in buffered saline solution, is deposited on slides covered with the antigen films. After a few minutes, the slides are washed with saline and water and the increment of thickness is determined. Some of the results have been condensed in Table 1.

TABLE 1

SPECIFIC REACTION OF FILMS OF BOVINE ALBUMIN WITH RABBIT ANTIBODIES

Number of bovine albumin layers	Increase in thickness in A units after adsorption of antibovine albumin serum	Increase in thickness in A units after adsorption of antiegg albumin serum
1	39	4
2	57	4
4	104	−3
6	136	−8
8	149	

It is evident from the data that films of bovine albumin react in an unexpected way. The amount of adsorbed antibody molecules increases with the number of underlying layers of bovine albumin up to four double layers. Thickness increments of antibodies obtained with five underlying double layers are about the same as those obtained with four double layers.

Quite a different result is obtained with egg albumin. With films of this protein, the amount of adsorbed homologous antibodies is independent of the number of underlying layers of antigen. Constant increment of antibodies of about 20A is obtained and

[1] K. Landsteiner, "The Specificity of Serological Reactions," Cambridge, Harvard University Press, p. 262. 1945.

[2] A. Rothen and K. Landsteiner, *Jour. Exp. Med.*, 76: 437, 1942.

[3] A. Rothen, *Rev. Sci. Inst.*, 16: 26, 1945.

[4] K. B. Blodgett and I. Langmuir, *Phys. Rev.*, 51: 964, 1937.

no increase is observed upon treatment with a heterologous serum at the dilution used.

Further, the investigation of the screening action of films transferred on the slide on top of the antigen films brought out most surprising results, which are, in fact, the main object of this note. It can be seen from the data in Tables 2 and 3 that screens consisting of stearic acid or protein layers do not prevent considerable specific adsorption of antibodies. When the antigen films consist of three double layers of bovine albumin, a specific reaction still occurs in spite of a screen of four double layers of stearic acid. Analogous results were obtained with screens of octadecylamine and mixed screens of octadecylamine and stearic acid.

TABLE 2

SCREENING EFFECT OF STEARIC ACID LAYERS ON THE ANTIGEN-ANTIBODY REACTION

	Antigen films: 3 double layers of bovine albumin (50A)		Antigen films: 1 double layer of egg albumin (16A)	
Screen: Number of stearic acid layers	Increase in A units after adsorption of anti-bovine albumin serum	Increase in A units after adsorption of anti-egg albumin serum	Increase in A units after adsorption of anti-egg albumin serum	Increase in A units after adsorption of anti-bovine albumin serum
2	87	0	18	0
4	61	2	13	5
6	36	6	12	10
8	29	13		

TABLE 3

SCREENING EFFECT OF EGG ALBUMIN LAYERS ON BOVINE ALBUMIN-ANTIBOVINE ALBUMIN REACTION

Antigen: Number of bovine albumin layers	2	2	2	2	2	6	6
Screen: Number of egg albumin layers	2	4	6	8	10	6	10
Increase in A units after adsorption with antibovine albumin serum	41	28	17	9	0	86	58

The interpretation of these results now becomes important. Perhaps the most obvious explanation is that stearic acid or protein films have holes through which the antibody molecules can reach the antigenic film. Such an explanation, however, is scarcely satisfactory if one considers the closely packed structure of stearic films in relation to the size of the antibody molecule (molecular weight $\simeq$ 160,000). Furthermore, an extensive series of experiments carried out in this laboratory have shown that stearic acid films may act as a perfect screen for certain types of reaction. For instance, at the proper pH a layer of insulin molecules 150A thick[5] (molecular weight $\simeq$ 40,000) can be adsorbed on a slide covered by a layer of protamine. Nevertheless, a monolayer of stearic acid deposited on the protamine prevents subsequent adsorption of insulin molecules.

The following explanation of our results is offered tentatively. It is assumed that the effective range of action between a film of antigen and an antibody molecule might extend to an order of hundreds of A instead of a few A as in the case of forces between individual atoms. In order to achieve such a long range, it is considered possible that a field of force of greater magnitude might result from an integrated action of the many elementary units which build up the single large molecules of antigen and antibody in an orderly way. It is a matter of speculation how this field is realized, but it is not impossible that it could result along the lines indicated by London.[6] Under favorable conditions, the field of force of the antigen film could be enhanced as the number of layers is increased, which seems to occur in the case of bovine albumin films. The data reported above may thus be interpreted in the sense that no direct contact is necessary between a film of antigen and the corresponding antibodies to demonstrate a specific interaction.

If this interpretation is correct, it means that in the animal body the sphere of action of antibodies is much greater than commonly supposed. An interaction might even occur through a thin biological membrane.

ALEXANDRE ROTHEN

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[5] G. H. A. Clowes, "Recent Advances in Surface Chemistry and Chemical Physics," The American Association for the Advancement of Science, No. 7, p. 61. 1939.

[6] F. London, "Surface Chemistry," The American Association for the Advancement of Science, No. 21, p. 141. 1943.

METABOLISM IN DIABETIC COMA PRODUCED BY ALLOXAN[1]

IT has been observed that the injection of alloxan in rats will produce varying degrees of diabetes mellitus—even severe coma—which is similar to that seen in human beings.[2,3] Alloxan has, therefore, provided us with a valuable experimental tool, with which to study the metabolism in diabetic coma and the results of therapy.

In human diabetic coma there is a marked elevation in plasma inorganic phosphate which decreases rapidly, following administration of insulin.[4,5] The mechanism of this fall is still obscure. Studies on normal animals show that insulin causes a rise in acid-

[1] These studies were aided by a grant from the Committee on Scientific Research of the American Medical Association.

[2] J. S. Dunn and N. G. B. McLetchie, *Lancet*, 245: 384, 1943.

[3] R. E. Janes and C. E. Friedgood, *Endocrinology*, 36: 62, 1945.

[4] G. M. Guest and S. Rapoport, *Am. Jour. Dis. of Children*, 58: 1072, 1939.

[5] M. Franks, R. F. Berris, N. O. Kaplan and G. B. Myers. In preparation.

soluble phosphates in the liver.[6,7,8] The present investigation was undertaken to examine the relationship between plasma inorganic phosphate and the acid soluble phosphates of the liver in diabetic coma.

Long-Evans hooded male rats of 200 to 300 grams in weight were used. The experimental animals were fed an equal amount of a stock diet for one week prior to the time of injection with alloxan. Control animals were similarly fed for one week before sacrificing.

Alloxan was injected intraperitoneally in a single dose of 200 mgm per kilo of body weight. Following the administration of alloxan, all animals consumed the same quantity of the stock diet. Urines were tested daily for sugar and ketone bodies. Only those animals which were clinically in diabetic coma were used. Each animal exhibited Kussmaul respiration, was semi-conscious or totally unconscious, and the urine showed a four-plus sugar (5–10 per cent.) and a four-plus acetone. Those animals which attained this stage of diabetes between 70 to 80 hours after the injection of alloxan were employed, for reasons which will be described in subsequent reports.

All animals were fasted for a period of 16 hours, before they were sacrificed. Under sodium pentobarbital anesthesia, blood samples were drawn from the inferior vena cava, and a portion of the liver was immediately removed and rapidly frozen. Blood samples were then analyzed for sugar and inorganic phosphate and the liver was analyzed for glycogen and acid-soluble phosphates.

Table 1 includes values for normal animals, "alloxan refractive" animals and severe untreated comas. The term "alloxan refractive" animals refers to those rats which showed no response to the injection of alloxan, despite the fact that they were given the same dose as the other animals. In the severely comatose animals, there was noted a marked elevation of blood sugar and of plasma inorganic phosphate, whereas in the liver there was a decrease in total acid-soluble phosphate, in the 7-minute hydrolyzable and residual phosphates, and in glycogen, together with a rise in liver inorganic phosphate. The 7-minute fraction appeared to consist chiefly of the labile phosphates of adenosine pyrophosphate (adenosine diphosphate and adenosine triphosphate). The decrease in this fraction may be attributed to a diminution of the oxidative reactions resulting from lack of insulin.[9] It will be observed that neither the presence of alloxan nor of dietary restriction per se accounts for the changes in the comatose animals.

TABLE 1*

	Number of rats	Blood sugar mgm per cent.	Plasma inorganic P mgm per cent.	Liver				
				Glycogen per cent.	Total acid soluble P†	Inorganic P	7-minute hydrolyzable P‡	Residual P§
Control animals	8	115 ± 2.4	8.7 ± 0.5	0.155 ±0.018	95.9 ± 2.2	24.2 ± 0.8	18.0 ± 0.6	54.1 ± 1.9
Alloxan refractive animals	5	105 ± 15.5	8.1 ± 0.7	0.128 ± 0.021	95.1 ± 1.4	23.3 ± 0.7	20.6 ± 1.1	51.6 ± 1.9
Comatose animals	6	770 ± 95.5	26.3 ± 2.4	.064 ± .013	73.4 ± 0.6	33.2 ± 1.3	6.2 ± 0.4	34.4 ± 2.1

* The measure of variability is the standard error of the mean.
† All liver P values are in mgm P per 100 grams of fresh liver.
‡ Consists chiefly of the labile P of adenosine pyrophosphate (mixture of adenosine triphosphate and adenosine diphosphate).
§ Residual P represents the difference in P after the 7-minute hydrolyzable and inorganic P have been subtracted from the total acid soluble P.

Table 2 gives the results when varying doses of insulin[10] are administered to the comatose rats. It is evident that such administration is followed by a significant fall in blood sugar and plasma inorganic phosphate. In addition there is a slight fall in the liver inorganic phosphate and an increase in the total

TABLE 2

EFFECT OF INSULIN THERAPY ON RATS IN DIABETIC COMA

Units* of regular insulin given intraperitoneally	Blood sugar mgm per cent.	Plasma inorganic P mgm	Liver				
			Glycogen per cent.	Total acid soluble P	Inorganic P	7-minute hydrolyzable P	Residual P
10	370	21.9	0.219	80.0	28.2	12.4	39.6
10–10	...	23.6	0.895	87.6	28.0	15.7	43.9
20–20	105	7.1	0.920	87.9	23.6	17.0	47.3
15–15–15	685	19.6	0.341	74.9	29.9	10.0	35.0
15–15–15	297	15.4	0.770	75.0	24.5	11.7	38.8
15–15–15	90	12.0	0.894	86.5	23.1	14.9	48.5
15–15–15	32	10.8	0.340	96.6	28.2	17.6	50.8
15–20–20	64	3.2	0.820	83.3	28.2	14.4	41.9
20–20–20	790	20.5	0.535	75.5	32.2	11.8	41.5
20–20–20	87.5	9.8	0.955	86.3	26.1	16.1	44.1
20–20–20	185	18.6	0.930	80.5	29.0	10.0	41.5

* Insulin was given every 1½ hours. The animals were sacrificed 1½ hours after the final dose.

[6] N. Nelson, S. Rapoport, G. M. Guest and I. A. Mirsky, *Jour. Biol. Chem.*, 291, 1942.
[7] N. O. Kaplan and D. M. Greenberg, *Am. Jour. Physiol.*, 140: 598, 1944.
[8] N. O. Kaplan and D. M. Greenberg, *Jour. Biol. Chem.*, 156: 525, 1944.
[9] N. O. Kaplan and D. M. Greenberg, *Jour. Biol. Chem.*, 156: 553, 1944.
[10] Insulin was generously supplied by Dr. W. A. Feirer, of Sharp and Dohme, Inc.

acid-soluble phosphate as well as the 7-minute hydrolyzable and residual phosphates. A marked rise in liver glycogen and considerable improvement of the clinical status of the animals was also noted. It is important to emphasize that enormous doses, up to 60 units of insulin, were necessary to bring about these improvements in comatose rats. It will be seen that although the degree of the response was not uniform the trends are definite.

SUMMARY

Alloxan given parenterally produces in the rat a state of diabetic coma which is analogous to the severe coma of human diabetes. Such animals, moreover, show a rise in plasma inorganic phosphate and blood sugar. They also show in the liver a decrease in glycogen and in the total acid-soluble phosphates. An increase in liver inorganic phosphate occurs with a concurrent fall in adenosine pyrophosphate and other organo-phosphates. Hence the rise in plasma inorganic phosphate during coma is at least partially due to a loss of liver phosphate. It is probable that this rise in plasma inorganic phosphate results from a breakdown of organo-phosphates which result from the depressed oxidations associated with insulin lack. Insulin, when administered in exceptionally large doses, tends to cause improvement in both the clinical and chemical state of comatose rats.

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AN EPIZOOTIC OF PNEUMOCOCCUS TYPE 19 INFECTIONS IN GUINEA PIGS[1]

OUTBREAKS of pneumococcal infections among guinea pigs have been known for some time to occur in this country and in Europe.[2] The epidemic strains and the pneumococci found in normal guinea pigs have not usually been classified serologically and those that were fell into the so-called Group IV. In 1932, Neufeld and Etinger-Tulczynska[3] identified the type 19 pneumococcus as the prevalent type in both healthy and infected guinea pigs of various laboratories and dealers in Berlin and elsewhere in Germany. At that time Webster could not find this organism in the nasal washings of guinea pigs in New York.[3] To our knowledge carriers of type 19 pneumococci or spontaneous infections with this organism have not been described among guinea pigs in the United States.[4]

The infections reported in this paper occurred among apparently healthy guinea pigs in the course of studies of certain effects of sodium salicylate in these animals. The occurrence of unexpected deaths among experimental and control animals prompted a bacteriological study which revealed that the type 19 pneumococcus was the cause of most of the fatal lesions. In addition, carriers of the same organism were found among apparently healthy guinea pigs. Sulfadiazine was used prophylactically in one group of animals in an attempt to eliminate the infections and to clear the carrier state.

Materials and Methods. The 3 groups of guinea pigs used in this study were procured from different dealers in widely separated localities. They were apparently healthy when received and no infections had previously been recognized in the stock from which they came. Nasal washings were obtained for culture in the first group as soon as the epizootic was recognized. In the other 2 groups they were done when the animals were first observed. These cultures were repeated at autopsy and, in addition, cultures were made from swabbings of the cut surfaces of the lungs, of the internal ears, nasal accessory sinuses and other purulent foci at that time. The nasal washings were done as described by Neufeld,[2] saline being used for the washings in the first group and broth in the other groups. The cultural methods for isolation and identification of the pneumococci were those described elsewhere.[1] Autopsies were done as soon as possible after the death of the animals or immediately after they were sacrificed (by stunning). Flamed instruments were used to cut the lungs and to open the bony structures before taking the cultures. The organs were examined grossly and also microscopically from Zenker's-fixed, paraffin sections stained with hematoxylin-eosin. The sodium salicylate and the sulfadiazine were fed to the animals by stomach tube, a separate tube being used for each animal. Their diets were not otherwise controlled. Cultures of the rabbit chow used to feed the animals yielded no pneumococci. The observations in each of the 3 groups will be presented separately.

Group I. The 20 guinea pigs in this group were delivered to the animal quarters at the Harvard Medical School on February 5, 1945, from a breeder in Saugus, Mass., which is about 10 miles north of Boston. After a few days they were brought to the animal house of the Neurological Unit at the Boston City Hospital, where they were kept thereafter in a

[1] From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital and the Department of Medicine, Harvard Medical School, Boston, Mass.

[2] For a review of the epidemiology of pneumococcal infections in animals see M. Finland, *Medicine*, 21: 307, 1942.

[3] F. Neufeld and R. Etinger-Tulczynska, *Ztschr. f. Hyg. u. Infektionkr.*, 114: 324, 1932.

[4] In 1938, Geoffrey Rake (*Am. J. Hyg.*, 28: 377) described spontaneous infections due to *S. enteritidis*, type 19 pneumococcus and *A. bronchosepticus* in a guinea pig breeding colony at the farm division of the Connaught Laboratories in Toronto.

single cage. As part of an experiment, 10 of these animals were given daily feedings of sodium salicylate by stomach tube and the others were being kept as normal controls.

A few days after the experiment was started, 6 of the treated animals died in rapid succession and large hemorrhagic areas were found in their lungs. These were thought at the time to be due to aspiration of the intubated material. Shortly thereafter, 3 control animals died and had similar pulmonary lesions. The possibility of an epizootic was then considered and cultures were made from the lungs of the next animal that died. These yielded type 19 pneumococci in almost pure culture.

Nasal washings of the 10 surviving animals were then cultured and the same organism was identified in only one of them. None of these animals showed any evidence of illness at this time and they were still kept in the same cage. Deaths occurred in 4 more animals from 5 to 9 days later and the same type of pulmonary lesion was found in each instance. In addition, one of them had bilateral purulent otitis and pleuritis and also pericarditis and another had pericarditis and multiple pulmonary abscesses. The only manifestations of illness in any of the animals were apathy and anorexia for 2 days before death. When the last of these animals died, the 6 survivors were sacrificed, but only 1 of them showed any significant pulmonary lesions. Type 19 pneumococci were found from one or more cultures in all but one of the animals that died and from 4 of 6 that were sacrificed. They were grown from the lungs of 4, the ears and sinuses of 6, the pleural exudates of 1 and the blood of 1. Many other organisms, notably gram positive and gram negative bacilli, staphylococci and indifferent streptococci were also found but were not considered to be significant.

Group II. On April 9, 1945, 4 days after the preceding experiment was terminated, 20 guinea pigs were received at the animal quarters of the Harvard Medical School from a dealer in Canton, Mass., which is about 15 miles south of Boston. Nasal washings from these animals were made and cultured on the following day and type 19 pneumococci were obtained from 4 of them. The guinea pigs were all brought to the same animal house at the Boston City Hospital, where the carriers were isolated and the remaining guinea pigs were kept together in a single large cage in a different room from the one previously used. All the animals appeared to be in perfect health.

The previous studies with sodium salicylate were repeated and, in addition, both the treated and control animals were given daily doses of sulfadiazine by stomach tube in an attempt to prevent and control the infections. A separate tube was used for each animal. Satisfactory sulfadiazine blood levels were maintained. Cardiac blood taken 24 hours after a dose showed levels ranging between 5.4 and 9.5 mgm of free drug per 100 ml. In spite of these precautions 2 animals died, one after 14 and the other after 20 days. Neither of them originally had positive nasal cultures. Type 19 pneumococci were obtained from cultures of the lungs and nasal washings at autopsy in one, but this organism could not be recovered from the other; although the latter had pneumonia of one lobe. The remaining animals were all sacrificed between the fifteenth and twenty-second days. Bronchitis, peribronchitis and focal bronchopneumonia were found in 4 of these animals.

Type 19 pneumococci were found at autopsy in 9 animals. They were found in nasal washings in 6, in the lungs of 3 and in the nasal accessory sinuses in all 9 of them. Among the 4 original carriers, it was found at autopsy in the nasal washings and sinuses of one and from the latter site alone in another.

Group III. This group consisted of 16 guinea pigs which were delivered on May 4, 1945, directly to the animal rooms of the Thorndike Memorial Laboratory from a breeder in Lenox, Mass., about 135 miles west of Boston. The animal rooms were in a different building from those of the Neurological Unit and were in charge of a different attendant. The animals were apparently in good health and showed no external evidence of infection. Nasal washings were done with broth soon after these animals arrived. These were cultured and inoculated into mice. Type 19 pneumococci were obtained from cultures of 7 of these animals and in 2 of them these organisms were grown in almost pure culture.

Summary and Conclusions

An outbreak of respiratory infections among guinea pigs occurring in the late winter and early spring of 1945 is described. The type 19 pneumococcus was identified as the organism responsible for the fatal lesions. The same organism was found in the respiratory tract of other apparently healthy guinea pigs obtained from three breeders in widely separated localities in Massachusetts. Although the type 19 pneumococcus has previously been found to be widespread in healthy and infected guinea pigs in Germany, this is probably the first time this organism has been identified under similar conditions in the United States. Sulfadiazine appeared to control the infections, in part, but did not eliminate the carrier state.

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THIOURACIL IN THE PREVENTION OF EXPERIMENTAL DIETARY CIRRHOSIS OF LIVER[1]

IN the light of recent extensive studies on animals, the ratio $\frac{\text{Methionine}}{\text{Cystine}}$ may be considered as the leading etiologic dietary factor in the prevention or production of liver cirrhosis.[2] Increased intake of methionine has a beneficial effect, whereas greater relative supply of cystine accelerates the appearance of cirrhotic changes in the liver of rats. In all these experiments the amount of both methionine and cystine in the diet is kept within physiological limits. The injury caused by cystine can be overcome not only by methionine, but by choline as well.

The prominent part played by the sulfur-containing amino acids, methionine and cystine, in the pathogenesis of hepatic cirrhosis, stimulated the investigation of the properties of other organic sulfur compounds.

In preliminary investigations, carried out in 1942, thiourea was given to rats in doses of 50 mg daily as supplement to a cirrhosis-producing diet containing Casein (SMACO) 8, Crisco 38, sucrose 48, salt mixture 4, cod liver oil 2, with the daily addition of thiamine (20 γ), riboflavin (25 γ), pyridoxine (20 γ) and Ca. pantothenate (100 γ). Thiourea proved to be poisonous, with death within 24 hours[3]—in a large number of the experimental animals. In many of the surviving rats the food intake remained low with rapidly progressive loss in weight. In view of these complications no definite conclusions could be reached, although the observations at autopsy in rats that survived 100 to 150 days seemed to indicate a distinct prophylactic effect of thiourea on liver cirrhosis.

With the recognition of thiourea and similar compounds, such as thiouracil, as specific drugs which interfere with the formation of thyroxine in the thyroid gland,[4] their possible relation to hepatic injury required further study. It is well known that in man lesions of the liver are common in hyperthyroid conditions. Conversely, it could be anticipated that lowering of the thyroid function achieved by thiourea, thiouracil and similar compounds might have a beneficial effect on the liver, perhaps owing to the decreased metabolic rate, including the metabolism of methionine.

Two sets—14 each—of adult male rats were put on the following diet: Casein (SMACO) 8, Crisco 38, sucrose 50, salt mixture 4, with 0.1 per cent. thiouracil in one group and no thiouracil in the other. Vitamins were given as supplements: thiamine (20γ), riboflavin (25 γ), pyridoxine (20 γ), Ca. Pantothenate (100 γ) daily and three drops of percomorph oil with 5 mg of mixed tocopherols (Distillation Products) weekly. In addition each animal in both groups received 50 mg of cystine daily with the purpose of accelerating and aggravating the cirrhotic changes in the liver. As customary, the experimental period was 150 days and those rats that survived were then killed. The final diagnosis of hepatic injury was based, without exception, on microscopic examination. Minor but definite cirrhotic changes were given the connotation of one +, whereas more severe cirrhosis was defined as ++ to ++++, with proper consideration for its varying degree in different lobes.

From the tabulation of all the pertinent data collected (Table 1) it becomes evident that admixture

TABLE 1

Group (Each 14 animals)	Weight loss		No weight loss	Dead before 150 days	Killed at 150 days	Fluids in serous cavities	Cirrhosis		
	> 50 gm	< 50 gm					0	+	++ to ++++
A. Without thiouracil	9	3	2	12	2	5	1	3	10
B. With thiouracil	5	1	8	2	12	..	9	4	1

of thiouracil to the basic cirrhosis-producing synthetic diet exerts a marked preventive effect, manifesting itself not only in much lower incidence and in milder degree of cirrhosis, but also in absence of serous effusions in the peritoneal, pleural and pericardial cavities, in better survival rate and in more satisfactory weight curves. The thyroid glands in all rats of group B showed, in the gross and microscopically, the typical picture of hypertrophy and hyperplasia caused by thiouracil.[5]

The beneficial effect of thiouracil in these experiments could not be explained by major differences in food intake. Beginning with the fourth experimental week the food intake was measured in 5 to 6 animals in each group. The tabulation on page 452 gives the daily averages (in gram) per week.

The beneficial effect of thiouracil (0.1 per cent. in the diet) on the prevention of cirrhosis of the liver and concurrently on the general well-being of the

[1] This investigation was aided by a grant from Wyeth Incorporated.

[2] See literature, P. György, *Am. Jour. Clin. Path.*, 14: 67, 1944.

[3] See also J. B. Mackenzie and C. G. Mackenzie, *Proc. Soc. Exp. Biol. and Med.*, 54: 34, 1943.

[4] J. B. Mackenzie, C. G. Mackenzie and E. V. MacCollum, SCIENCE, 94: 518, 1941; C. G. Mackenzie and J. B. Mackenzie, *Endocrinology*, 32: 185, 1943; E. B. Astwood, J. Sullivan, A. Bissell and R. Tyzlowitz, *Endocrinology*, 32: 201, 1943; E. B. Astwood, *Jour. Am. Med. Asn.*, 122: 78, 1943; R. H. Williams and G. W. Bissell, *New England Jour. Med.*, 229: 97, 1943.

[5] C. G. Mackenzie and J. B. Mackenzie; E. B. Astwood, J. Sullivan, A. Bissell and R. Tyzlowitz: *cf.* 3 lc.

Group A (No thiouracil)	Rat 40*:	6.6	8.2	7.4	7.3	7.3	7.0	6.7	7.7	6.5	5.9	5.5	4.8	4.2	2.6†		
	Rat 43*:	8.3	9.7	9.4	9.2	8.5	7.5	6.3	9.2	2.9†							
	Rat 44*:	9.0	11.2	11.7	12.2	10.8	9.7	7.0	9.4	7.6	6.3	7.0	6.0†				
	Rat 45*:	8.6	10.4	10.0	8.1	9.0	8.3	7.3	10.2	8.0	6.0	6.2	5.1	5.1	4.8	4.1	3.4	0.7†
	Rat 53*:	5.2	6.9	6.6	5.9	6.3	6.3	5.4	6.4	5.3	1.4	4.4	4.4	5.5	2.7	2.3	2.0†
	Rat 68*:	6.3	7.4	7.4	6.7	6.4	7.6	6.5	7.7	6.4	7.0	7.4	6.9	8.4	6.0	5.2	6.3	6.5†
Group B (With thiouracil)	Rat 55**:	8.8	7.8	6.6	5.6	5.8	6.5	6.2	6.6	6.7	6.3	7.1	7.4	7.9	7.5	7.3	7.1	7.4†
	Rat 59‡:	6.1	5.7	7.0	6.8	6.6	8.0	5.7	7.6	6.2	6.1	5.9	5.6	6.4	7.5	5.8	6.3	7.7†
	Rat 60‡:	7.2	6.9	6.6	7.0	6.6	4.9	4.5	7.5	6.7	6.0	5.7	5.2	5.9	6.7	5.8	6.6	6.1†
	Rat 63‡:	6.6	6.1	6.4	6.3	5.9	6.0	4.7	8.0	6.2	6.1	6.5	6.4	6.0	6.1	7.4	7.9	8.1†
	Rat 64‡:	6.6	7.2	7.0	5.1	5.5	6.3	5.7	6.4	5.9	6.5	5.5	5.5	5.5	6.4	6.5	7.7	8.6†

* Cirrhosis.

** Mild cirrhosis.
‡ No cirrhosis.

Average daily food intake Group A: 6.7 gm.
Group B: 6.5 gm.

animals kept on a severe cirrhosis-producing regime is in good accord with the protective action of sulfanilamide against the hepatic cirrhosis due to chronic poisoning with carbon tetrachloride.[6] Both sulfanilamide and thiouracil inhibit the formation of thyroxine in the thyroid gland[5] and their effect on the liver might be based on this common denominator. Methionine protects the liver not only from purely dietary (trophopatic)[7] but also from postnecrotic (toxipathic)[7] cirrhosis, such as is caused, for instance, by carbon tetrachloride.[8] It can be assumed that the possible saving effect of lowered metabolic rate on methionine may, therefore, manifest itself not only in trophopathic but also in toxipathic cirrhosis.

The clinical implications of the above observations are obvious: Thiouracil presents itself as a supporting measure in the treatment of cirrhosis in combination with a diet rich in protein and methionine. The high incidence of injurious manifestations following thiouracil therapy does not militate against its use in cirrhosis for which condition any possible improvement in prognosis, even if only on account of prevention of progress of the disease, would represent a distinct advantage. Constant clinical observation, with repeated blood counts (leukopenia), is indispensable. It may be surmised that jaundice, seen in very few cases as a toxic complication of thiouracil medication in the clinic, is more the expression of allergic reaction than direct hepatic injury. How far these experiments on animals will prove to be valid in therapeutic clinical studies, only experience will teach.

Conclusions. Thiouracil mixed to a cirrhosis-producing synthetic diet in amount of 0.1 per cent. has a preventive effect on the production of cirrhosis in rats.

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[6] J. C. Forbes, B. E. Leach and G. Z. Williams, *Proc. Soc. Exp. Biol. and Med.*, 51: 47, 1942.

[7] H. P. Himsworth and L. E. Glynn, *Lancet*, I: 457, 1944.

[8] P. György, J. Seifter and R. M. Tomarelli. Unpublished experiment.

SCIENTIFIC APPARATUS AND LABORATORY METHODS

THE APPLICATION OF GEOPHYSICAL OSCILLOGRAPHS TO MULTIPLE RECORDINGS IN PHYSIOLOGY

THE simultaneous recordings of several physiological phenomena is facilitated by the use of appropriate pick-up units that convert the events into electrical signals which are capable of actuating galvanometers, oscillographs, inkwriters or other recording devices. When a number of phenomena such as blood pressure, respiration, blood flow, body temperature, the activity of the heart, the activity of nerve fibers, the contraction of muscles, etc., are to be accurately and simultaneously recorded, severe instrumental difficulties arise because of the variety of pick-up units that are required for the recording of these several phenomena. The ideal recorder should be compact, permanently aligned, sensitive; yet rugged and simple to operate. Under these conditions atten-

tion can be devoted to physiological problems being studied rather than to the care and maintenance of some make-shift apparatus. Geophysicists are able to make multiple recordings through the use of small, rugged and sensitive galvanometers aligned in banks of twelve or more and incorporated into compact, photographically recording oscillographs. These instruments are widely used in the recording of strains and vibrations in mechanical structures, in the detection of seismic disturbances and in a number of other physical and engineering applications. The galvanometers are ordinarily of the moving coil type and a variety of sensitivities are available from those giving a deflection of only a fraction of a millimeter per milliampere (at one meter optical distance) to others which give a 700–1,000 millimeter deflection per milliampere. The sensitivity of these galvanometers is inversely proportional to the square of the nattural frequency and a variety of galvanometers with a variety of frequency responses are obtainable. The most sensitive types have a natural frequency in the neighborhood of 40 c.p.s., while others going up to several thousand c.p.s. are also available. Oscillographs may be ordered which incorporate several types of galvanometers in one instrument, making possible the application of the most suitable galvanometer for a particular recording. It is of course necessary to employ a galvanometer having a response which is flat over the entire frequency range which is liable to be encountered in any one recording, but the frequency requirement should not be unnecessarily extended because of the lower sensitivity which is then obtained. Many features useful for the physiological laboratory are included in the various oscillographs, such as: paper speeds which may quickly be varied from a fraction of an inch per second to several feet per second; a built-in camera which does not require a darkened room for recording; a built-in timing system which places an accurately aligned time line completely across the record; and, in the more elaborate instruments, attenuators which individually control the galvanometers. Details of the galvanometers and oscillographs may be obtained from current geophysical literature, from texts[1] and from the technical data supplied by the companies making these instruments.

It is important to note that these galvanometers are low impedance instruments and the problem of feeding into them must be solved differently for the various pick-up units. If a low impedance input unit is employed, matching to the galvanometer is obtained and enough sensitivity may then be available so that no amplification is required. A low impedance device that is especially adapted for coupling to these galvanometers is the wire strain gage,[2, 3] which is now available commercially. There is no reason why the strain gage can not be applied to the recording of such physiological phenomena as blood pressure, intra-arterial pulse, isometric muscle contractions, etc. Use of the strain gage has already been made in recording the human finger pulse[4] and strains in the skull.[5] When high impedance pick-up units are used, special matching stages are required. The geophysical practice of using stepdown transformers is not possible in physiology because of the low frequencies often encountered, and special vacuum tube matching stages may be required. One useful method of matching is to include the galvanometer in a cathode follower circuit.[6] The authors have found a simple and satisfactory arangement to be two tubes in parallel as shown in the output stage of the amplifier of Fig. 1A. The load resistance is made equal to the internal

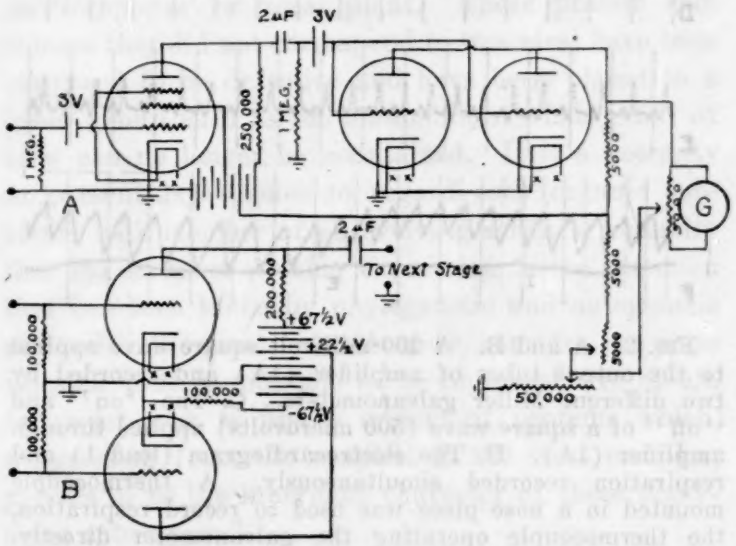

FIG. 1. A. A battery operated condenser coupled amplifier. The plate supply is 225–270 volts and the screen supply is 45 volts. B. Modification of Matthews' differential input stage using 6C6 as triodes. Other tubes, such as 6SC7, may be used.

resistance of the tubes. A fixed resistance equal to the load resistance is connected to ground through a variable resistance, which is several times the combined plate and load resistances. This arrangement eliminates the use of bucking voltages in balancing out the plate current. A second variable resistance may be added to serve as a finer balance control. The current that passes through the galvanometer is controlled by a variable potentiometer acting as a shunt. The output tubes are type 6C6 connected as triodes, but others, such as type 42, 6F6 or 6SC7, are

[1] J. J. Jakosky, "Exploration Geophysics," 1st edition, Times-Mirror Press, Los Angeles, California, 1940.

[2] D. M. Nielsen, *Electronics*, 16: 106, December, 1943.

[3] R. O. Fehr, *Electronics*, 18: 112, January, 1945.

[4] H. Grundfest, J. J. Hay and Sergei Feitelberg, SCIENCE, 101: 255, 1945.

[5] E. S. Gurdjian and H. R. Lissner, *Jour. Neurosurgery*, 1: 393, 1944.

[6] W. Richter, *Electronics*, 16: 112, November, 1943.

also satisfactory. Figs. 2A and 2B illustrate the responses of two different geophysical galvanometers (Miller) to a 200 millivolt signal applied to the grids of the output tubes. The current change is approximately 15 microamperes. With a single pentode (6C6) RC-coupled to the output tubes to provide amplification (Fig. 1A), a 500 microvolt signal gives a good deflection, as shown in the records (Fig. 2C) obtained in response to the "on" and "off" of a 500 microvolt square wave. The voltage amplification, as measured with the cathode ray oscillograph, is about 100. The time constant of this amplifier is about 1.5 seconds, but this figure could be increased by the use of a double RC coupling[7]; or even direct coupling could be employed. The ability of this amplifier and the Miller galvanometers to record such physiological processes as the electrocardiogram and finger pulses is shown in Fig. 2 (D, E, F). The finger pulse records are similar to those taken with the cathode ray oscillograph.[8]

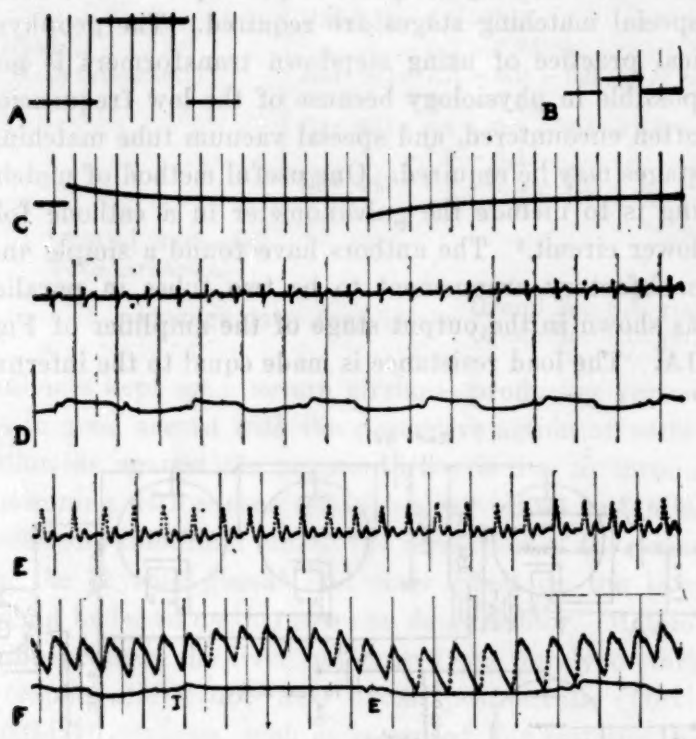

FIG. 2. A and B. A 200 millivolt square wave applied to the output tubes of amplifier (1A) and recorded by two different Miller galvanometers. C. The "on" and "off" of a square wave (500 microvolts) applied through amplifier (1A). D. The electrocardiogram (lead 1) and respiration recorded simultaneously. A thermocouple mounted in a nose piece was used to record respiration, the thermocouple operating the galvanometer directly. Upward deflections represent inspiration. E. Pulse in the right index finger recorded by the use of the hot wire-thermocouple method.[6]. F. Pulse in the right finger recorded by means of a phototube and showing the effects of a prolonged inspiration (beginning at I) and the effect of a prolonged expiration (beginning at E). Time throughout is in half seconds.

The special advantage of these geophysical galvanometers is that they combine, as few other galvanometers do, the qualities of sturdiness, sensitivity and good frequency response. Many pick-up units such as strain gages, thermocouples, thermopiles, photocells, etc., can be used either coupled directly to the galvanometer or through a simple matching stage. This makes unnecessary the need of high-gain amplifiers, which, especially in the low frequency (subaudio) range, involve special design problems or special precautions in order to achieve a reasonable degree of stability. For some types of physiological recording it may be necessary to utilize a balanced or differential input stage. Quite adequate is Matthews's[9] circuit employing two tubes with a common cathode resistor and a negative cathode voltage. A slightly modified arrangement (Fig. 1B) is very satisfactory and possesses a high differential action. When added to the amplifier (Fig. 1A) the total voltage amplification is about 1,000, and 50 microvolts gives a good deflection.

It would seem that the use of these oscillographs in physiology would simplify many instrumental problems and give to the physiologist and biologist a convenient and useful tool for simultaneous multiple recording of many physiological changes in either one or several organisms.

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DISCUSSION

THE AMINO ACID COMPOSITION OF PROTEINS

IN a recently published monograph on methods for the amino acid analysis of proteins,[1] the practice is advocated of computing the results of the determinations upon the uniform basis of a hypothetical substance that contains 16 per cent. of nitrogen. Comprehensive tables of data are presented, in all of which the original figures from the literature have been recalculated. The authors state that this is done

[1] R. J. Block and D. Bolling, "The Amino Acid Composition of Proteins and Foods." Springfield, Illinois. 1945.

[7] F. E. Terman, *Radio Engineers' Handbook*, 1st edition, p. 374. McGraw-Hill Book Co., Inc., New York, 1943.

[8] F. Crescitelli and E. Gardner, *Jour. Lab. Clin. Med.*, 30: 63, 1945.

[9] B. H. C. Matthews, *Jour. Physiol.*, 93: 25P, 1938.

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"in the interest of uniformity and to facilitate comparison," but they fail to explain why they think, for example, it is easier to compare the results of the analysis of casein, a substance that contains close to 15.7 per cent. of nitrogen, with similar results for edestin, which contains about 18.7 per cent., after both groups of data have been recalculated in this way. Actually, this procedure gratuitously introduces an element of inaccuracy. It is the equivalent of suggesting that, prior to analysis, protein preparations of nitrogen content greater than 16 per cent. should be diluted with sufficient non-nitrogenous material to reduce the average nitrogen content to this level, while protein preparations of lower nitrogen content should be in some way fortified with nitrogen. The values for the percentage yields of amino acids determined by analysis are thus distorted, this distortion being the greater the more the actual nitrogen content of the preparation deviates from the assumed 16 per cent.

Proteins are regarded by most investigators as comprising a fairly clearly defined category of organic substances, although their properties and their composition with respect to constituent amino acid residues may vary within extremely wide limits. The well-known differences in their nutritive effect in the animal body are made neither more nor less striking if the composition is expressed in the manner described, nor is the basis of any of their properties save nitrogen content thereby equalized. It has never been suggested that the consideration of any other broad group of organic substances would be facilitated if the composition were expressed upon an analogous artificial basis. Why, then, should the proteins receive so unusual a treatment?

It is possible that the suggestion has its origin in the convention which has long been employed, in the absence of information upon the actual nitrogen content of the proteins in a solution or tissue, that an approximation to the weight of the protein present may be secured by multiplying the nitrogen content of the solution or tissue by the factor 6.25. This treatment assumes that the proteins contain, within the limits of accuracy desired, 16 per cent. of nitrogen. Aside from the protamines and certain seed globulins, which are especially rich in arginine, there are few proteins that contain more than 18 per cent. of nitrogen. Also, with the exception of certain complex materials, many of which appear to be associations or compounds of protein with lipides or with carbohydrates, there are few protein preparations that, in a satisfactorily purified condition, contain much less than 15 per cent. of nitrogen. Accordingly, the use of the conventional factor would give a result about 11 per cent. too high in the case of a protein that actually contained 18 per cent. of nitrogen, and about 6.5 per cent. too low if it contained 15 per cent. For some purposes, such a range of uncertainty is not objectionable, and many proteins of importance in animal biochemistry do not differ widely in nitrogen content from the 16 per cent. that is assumed. Nevertheless, the magnitude of the error may become serious with such substances as gelatin or silk fibroin and especially when proteins of vegetable origin are under consideration. This last point was carefully emphasized by Ritthausen[2] as long ago as 1872 and was discussed thoroughly by Jones[3] in 1931.

In 1901, Kossel[4] delivered a lecture before the German Chemical Society, which he concluded with the following statement. "It has been customary to think of protein as a substance of definite fixed properties, a sort of 'ideal protein' much as Goethe thought of an *'Urpflanze'* or 'ideal plant.' Those protein substances that did not correspond to this ideal have been supposed to be defective and have been placed in a lower group such as the albuminoids. This point of view can no longer be maintained. It is a necessity in present-day science to regard each organic substance as a member of an evolving series, a necessity that has its most striking expression in the direction that has been taken by phylogenetic and ontogenetic research. We must not, therefore, consider one complicated protein molecule to be representative of all, but must seek to find a system of proteins which, progressing from the simplest to the most complex, reveals to us the innermost character of these many-sided substances."

It would seem that the recalculation of the amino acid composition of all proteins, whatever their nitrogen content, upon the arbitrary basis that has been suggested is a return to the point of view objected to by Kossel and represents a step that, as long as forty-five years ago, he would have regarded as a backward one. The data of the protein analytical chemist are to-day finding application in many directions. They are used for the characterization and differentiation of proteins, for the study of their molecular composition, in the interpretation of their chemical and physical properties, in studies of metabolism and of protein nutrition, and they will doubtless find ultimate use in the explanation of the enzymological and immunological properties of proteins

[11] Now with the Medical Research Laboratory, Edgewood Arsenal, Edgewood, Maryland.

[2] H. Ritthausen, "Die Eiweisskörper der Getreidearten, Hülsenfrüchte und Ölsamen," p. 236. Bonn: Max Cohen u. Sohn. 1872.

[3] D. B. Jones, U. S. Dept. Agric. Circular 183, 1931.

[4] A. Kossel, *Ber. chem. Ges.*, 34: 3214, 1901.

and in the development of a comprehensive theory of protein structure. These are fields of great activity in biochemistry, and in all of them the demand is for accuracy and more accuracy.

The employment of a method of calculation which introduces needless error without any compensating advantage is strongly to be condemned. This is not the time for a backward step, for a relaxation of the standards of accuracy or for the introduction of a new complication into an already sufficiently complex situation.

Attention is drawn to this matter because several papers have recently appeared in which the use of the proposed method of calculation has apparently escaped the vigilance of the referees, and more are to be anticipated.

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RELATIONSHIPS OF LYMPHOCYTES AND CANCER[1]

FINDING a direct correlation between the amount of lymphoid tissue in the intestine and the incidence of spontaneous mammary tumors in several pure strains of mice[2] suggested the idea that the lymphocyte might contribute to the growth of tumors or possibly even to instigate them. Lymphocytes have been considered in many studies on cancer, but practically all the experiments have been designed from the viewpoint that this cell and the lymphoid tissue has a part in immunity to tumor transplants. The conclusions obtained have not been consistent, one group of investigators maintaining that the lymphocyte is a factor to immunity; the other, that this cell has no part.

The approach used here is based upon histological association between the presence of lymphocytes and tumors and also upon correspondence in the growth and incidence of tumors and conditions that result in an increase or decrease in the number of lymphocytes within a tissue or throughout the body as a whole.

Mammary tumors. Records of metastases of mammary carcinoma in women and data obtained from animal experiments indicate a connection between mammary tumors and the presence of lymphocytes. Metastases of mammary carcinoma occur most frequently in lymph nodes, organs normally composed chiefly of lymphocytes. In addition, lymphocytes are present in metastases to the liver,[3] in neoplastic foci developed from burst lymphatics[3] and between the elastic connective tissue and the epithelium containing neoplastic cells in Paget's disease of the nipple.[4]

Animal experiments indicate several histological associations between lymphocytes and mammary tumors. The mammary tumor inciter in mice has been found in the milk, blood, spleen, thymus, lactating mammary tissue and breast tumors of certain strains high in their incidence of spontaneous mammary tumors.[5, 6] No cell is as numerous in all these fluids and organs as is the lymphocyte; it is a dominant histological element in the spleen and thymus gland. Furthermore, lymphocytes occur in the milk of many animals and have also been identified in the stomach contents of nursing mice. After centrifuging milk diluted with saline, the lymphocytes occur chiefly in the sediment, very few remaining in the supernatant fluid. The milk factor in mice has been found to be concentrated in the sediment.[7]

Breeding in pure strains of mice shows another connection between the incidence of spontaneous mammary tumors and lymphocytes. For example, strain dba has only 51 per cent. tumor incidence in virgins, but 85 per cent. in the breeding females; strain A shows a more marked difference by having less than 5 per cent. in virgins and 84 per cent. in breeding females.[8] One prominent histological change in the mammary gland during pregnancy and lactation is the presence of quantities of lymphocytes. There are masses of lymphocytes in the mammary gland of mice belonging to line dba during various stages of pregnancy and lactation.[9]

Lymphocytosis. The term "lymphocytosis" as used here will apply not only to an increase in the circulating lymphocytes, but also to an increase in the number of lymphocytes within an organ or tissue.

Data exist to show that one inciter of tumors is irritation, whether it be caused by chemicals, physical factors, radiation or possibly by certain parasites and viruses. Regardless of its source, irritation produces histological changes involving the attraction of the white blood cells. Lymphocytes are present at neoplastic foci caused by irritation.

The increase in blood lymphocytes that occurs in some unbalances of the endocrines and in some in-

[1] The author is a recipient of a Finney-Howell Research Fellowship.

[2] M. A. Kelsall. Paper in press.

[3] W. S. Handley, "Cancer of the Breast and Its Treatment." New York: Hoeber. 1922.

[4] G. L. Cheatle and M. Cutler, "Tumors of the Breast." Philadelphia: Lippincott.

[5] J. J. Bittner, *Trans. and Stud., College of Physicians of Philadelphia*, 4 ser., 9: 129–142, 1941.

[6] G. W. Woolley, L. W. Law and C. C. Little, *Proc. Nat. Acad. Sci.*, 29: 22, 1942.

[7] C. P. Barnum, Z. B. Ball, J. J. Bittner and M. B. Visscher, SCIENCE, 100: 575, 1944.

[8] C. C. Little, "Biology of the Laboratory Mouse." Philadelphia: Blakiston. 1941.

[9] E. Fekete, personal communication, 1945.

fectious diseases also indicates a positive relationship between lymphocytes and tumor growth. The sex hormones are known to be a factor in tumor production; unbalance of the sex hormones has been found to stimulate growth of lymphoblastic tissue.[10] Lymphocytosis occurs in some stages of syphilis, a fact that may account for the greater incidence of carcinoma of the lip in syphilitics.[11]

Lymphopenia. Not only are there correlations between an increase in the number of lymphocytes and increased incidence and growth of tumors, but there are also correlations between a decrease in the number of lymphocytes and decreased incidence and growth of tumors.

Chronic inanition decreases both the blood lymphocytes and the growth of tumors. Stern and Willheim state that "the prevailing majority of authors have expressed the opinion that food restriction is followed by depression of neoplastic growth."[12] Animal experiments give evidence to prove that the amount and kind of food affects the incidence of tumor development. No tumors occurred in C3H mice placed upon a diet in which the carbohydrates and fat were reduced to one third.[13] Inanition has been found by many authors to reduce the number of circulating lymphocytes and to cause involution of lymphoid organs.

Furthermore, observations have frequently been made that primitive societies are less well nourished and have a lower incidence of cancer[14] and also that cancer is less frequent among people having progressive tuberculosis,[14] a condition found by Sabin[15] to be accompanied by lymphopenia. However, the statistical significance of these observations has not been established.

The therapeutic effect of radiation agrees with the idea that a reduction in lymphocytes reduces tumor growth. Mottram[16] found that x-rays over a wide range of intensity caused a 50 per cent. decrease in the number of circulating lymphocytes, and Michels[17] found that the lymph nodes underwent fatty involution following x-rays.

Nucleus of the Lymphocyte. The most obvious characteristic of the small lymphocyte is its enormous nucleus in proportion to the amount of cytoplasm. No other cell in adults has a nucleus nearly as large in proportion to the cytoplasm except sperm, cells that are known to initiate the division of another cell. Basophilic staining reveals that most lymphocytes have larger nucleoli and contain more nucleic acid than most cells. Staining also shows that there are two kinds of small lymphocytes varying in their degree of basophilic staining. Stowell[18] thoroughly reviews the literature on the role of thymonucleic acid in tumors and concludes that a disturbance of the nucleoproteins forms the basis for an "intracellular cause of neoplasia." The lymphocyte may have a part in modifying nucleoproteins and be the source of the greater amount of thymonucleic acid found in carcinomas.[19]

There may also be a relationship between normal growth processes and quantitative chemical changes initiated by lymphocytes on the one hand, and abnormal growth and abnormal lymphocytosis on the other. The thymus gland has long been thought to have a part in normal growth; at the present time thymocytes are considered to be the same as lymphocytes. Lymphoid tissue involutes with age, the decrease being particularly coincident with the attainment of mature growth in the case of the thymus gland. In addition, those tissues of the adult that are most active mitotically contain large numbers of lymphocytes. The bone marrow continues production of blood cells throughout life and contains quantities of lymphocytes. During pregnancy the mammary gland of the adult is also subjected to rapid growth, a change accompanied by the invasion of lymphocytes into this organ.

Summary. Lymphocytes are present in metastases of mammary carcinomas, in tissues containing the mammary tumor inciter and at neoplastic foci caused by irritation. Unbalance of sex hormones stimulates lymphoblastic tissue and increases tumor incidence. Inanition and radiation reduce the number of circulating lymphocytes and also the growth and occurrence of tumors. The nucleus of the lymphocyte is considered to be a possible factor causing a disturbance of the nucleoproteins.

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[10] D. Marine and S. H. Rosen, *Proc. Soc. Exp. Biol. and Med.*, 44: 61, 1941.
[11] C. Ryall, *Brit. Med. Jour.*, 2: 697, 1913.
[12] K. Stern and R. Willheim, "Biochemistry of Malignant Tumors." Brooklyn: Reference Press. 1943.
[13] M. B. Visscher, Z. B. Ball, R. H. Barnes and I. Siversten, *Surgery*, 11: 48, 1942.
[14] H. Gilford, "Tumors and Cancers." London: Selwyn and Blount. 1925.
[15] F. R. Sabin, *Amer. Rev. of Tuberculosis*, 25: 153–171, 1931.
[16] J. Mottram, *Jour. Path. and Bact.*, 34: 800–801, 1931.
[17] N. A. Michels, *Amer. Jour. Anat.*, 57: 439–501, 1935.
[18] R. E. Stowell, *Cancer Research*, 5: 283–294, 1945.
[19] R. E. Stowell and Z. Cooper, *Cancer Research*, 5: 295–301, 1945.

WHAT IS EDUCATION AND WHAT IS DISPENSABLE?

THE suggestions offered by H. M. Dadourian[1] include two ideas which seem quite opposite. I fully

[1] H. M. Dadourian, SCIENCE, 101: 612, 1945.

concur as to the "pressure due to mounting scientific knowledge," but I look with suspicion upon proposals for streamlining education. Dadourian suggests elimination of everything which is not indispensable. He also suggests teaching of physical and biological sciences from kindergarten through high school. The latter should find favor with science teachers, but would it not be one of the dispensables of others?

The second group of suggestions which troubles me includes "greater use of the historical and philosophical approach." I have wanted to follow this but have been unable to see how to include it in courses already too short for fundamentals. "Greater use of the laboratory method" is also suggested, but I gather from slight exposures to the streamliners that this is a waste of time.

Many years ago a colleague expressed the opinion that there was too much duplication in education. My old-fashioned mind, impressed with the difficulties the modern generation has in simple sums and grammatical constructions, responded: "Yes. To-day we shall teach $2 \times 2 = 4$; to-morrow we must not repeat that, but teach something else."

I have long felt that learning should be regarded as a photographic process. A good impression is secured by using a fine stop and long exposure. The modern photographer reduces time by use of faster plates, and there are those who hold that modern methods of teaching accomplish a similar end. It is probably fortunate that we can not change the brain cells so easily. Nature slowly heals over the scars of volcanic eruption and those of devastating war. Two times two are still four; there still are 24 hours in each day; plants still synthesize the life-giving carbohydrates.

Some years ago I evolved a definition of education, *viz.*, "something to keep the child busy while he is growing up." I have been told that this is all wrong, that modern methods recognize definite goals and procedures. Perhaps this period is not "education." Perhaps education only begins with graduation from college. Perhaps it is largely extra-curricular. Many of our students profess to have discovered that it is so. In any case, we need to recognize that it differs greatly in individuals and in subjects. Differences in opinion are usually differences in interpretations. My definition could scarcely be training for a profession, and those who do not approve of it can easily hold that all education should be training for profession.

After more years of trying to participate in education, I still feel that my definition has some merit. I recall some pithy advice of another colleague of the old school: "It doesn't matter what courses you take. Pick out the best teachers and take the hardest courses they offer." My own son wrote to a leading law school to ask what undergraduate courses they would suggest. They recommended no specific courses but only that he take substantial ones and follow them through.

After some years of trying to use short cuts in laboratory biology, I find myself tending to revert to the old style requirement of making drawings, because they give longer exposures and opportunity to raise questions which cause students to begin to think and to consider what they are seeing. Others will no doubt succeed better with new methods. Good teachers are deplorably rare and too often are drawn into more lucrative fields.

The pressure due to mounting knowledge is very real. It is serious. Perhaps we wonder if we begin to see reasons why ancient civilizations decayed after reaching a high peak. I am a pessimist. It is difficult to be otherwise, faced with colossal waste of war, strife and bickerings, when there is crying need for reasonable cooperation. There are heartening signs of serious attempts to meet the present situation, and it should be possible to at least postpone general calamity.

Reasonable solution of present affairs will not relieve the pressure due to mounting knowledge. I have no panacea to offer, unless it be willingness to know less, to do less, to live more slowly and sanely. The streamliners and post-war adjustmenters would have us believe that they are solving problems, but when the smoke and dust have cleared away, even if our civilization tumbles, two and two will still make four, the sun will still shine and the earth will be green.

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SCIENTIFIC BOOKS

THE VELOCITY OF LIGHT

The Velocity of Light. By N. ERNEST DORSEY. 110 pp. Transactions of the American Philosophical Society, New Series. Vol. xxxiv, Part 1. 1944. $2.25.

THIS is something that has needed doing for a long time, and Dr. Dorsey has set a standard of rigorous and objective criticism that should serve as a model and guide for future workers in this field.

The nature of the problem to be considered is clearly stated in the introduction, and the suggestions concerning a secular variation of the velocity of light are

briefly reviewed. Unlike previous writers on this subject (including the reviewer), Dr. Dorsey does not base his discussion on the published definitive values given by the various observers. Instead, he points out that "the published definitive values, with their accompanying limits of uncertainty, are not experimental data, but merely the author's inferences from such data. Inferences are always subject to question; they may be criticized, reexamined and review at any time. When uncritically accepted, they form an exceedingly weak foundation for a revolutionary suggestion; in fact, the suggestion then rests solely on authority." Furthermore, the suggestion of a secular variation "cannot be satisfactorily attacked by merely pointing out that only slight changes in the admitted uncertainties of the measurements will render the suggestion unnecessary, especially if those changes must exhibit some kind of regularity. The most that can be accomplished by such criticism is to show the weakness of the foundation on which the suggestion rests, to show that the suggestion is unproven; whereas the critic presumably wishes to show that there is no basis at all for the suggestion."

Hence, Dr. Dorsey has undertaken to examine carefully the details of the work behind the published definitive values in order to independently appraise the objective value of the work in each case. His detailed discussion of the different investigations is prefaced by eight pages of remarks concerning the theory of errors, the method of least squares, averaging and absolute physical measurements. The treatment is original and stimulating and could very well be required reading for all who are concerned with precision measurements. In two valuable appendixes, Dr. Dorsey discusses (1) the experimental methods for determining the velocity of light and (2) motion maintained by periodic impulses.

All direct measurements of the velocity of light (denoted by V, instead of the customary c) are considered, with the exception of the work by Young and Forbes. The pioneer determinations by Fizeau and by Foucault are discussed briefly, but are not used to test the constancy of the velocity of light, owing to their great uncertainty. Cornu's work is very thoroughly discussed (22 pages) and a revised definitive value is calculated. Errors are found in the reductions of Perrotin and Prim, and Dorsey recomputes their value with corrected equations. Newcomb's work is shown to be affected by systematic errors of unknown sign and magnitude. Michelson's various determinations receive the most exhaustive (27 pages) and critical treatment of all. His reports are strongly criticized:

> Not one of his reports contains sufficient detailed information to enable a reader to form an independent and objective evaluation of the result. Whatever value he may attach to it is purely subjective, resting solely on his confidence in Michelson. . . . When details are given, they have to do with the simplest of measurements, those open to the least question. Of the more recondite measurements, those involving real difficulty and where mistaken procedures would not be especially surprising, little or nothing is said. . . . In none of his reports on the velocity of light prior to 1935 does one find any indication of a thorough experimental study of his apparatus and procedures.

The recent work by Karolus and Mittelstaedt, Anderson and Hüttel is perhaps too briefly presented, and without detailed criticism. The important question of the correction for "group velocity" is not satisfactorily handled, and it is to be hoped that Dr. Dorsey and others will look into this further.

Dr. Dorsey concludes that all determinations made prior to 1928 are of historical interest only, and bases his best value (299,773 km./sec.) on the mean of the Kerr cell determinations and the Michelson, Pease and Pearson determination. The actual uncertainty of this result (called the "dubiety") is thought to be perhaps as much as, but probably less than ±10 km./sec. Finally, it is concluded that "the data give no indication of any secular change in the velocity of light."

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THE LIFE HISTORY OF AN AMERICAN NATURALIST

The Life History of an American Naturalist. By FRANCIS B. SUMNER. vii + 298 pp. The Jaques Cattell Press, 1945. $3.00.

THE author, whose death closely followed the publication of this book, stated that his aim in writing his autobiography was a desire to bring to as wide a circle of readers as possible some of his long-cherished ideas relative to present-day beliefs and behavior. To this end he has analyzed his own personality and remembered experiences with the same impartiality that has characterized his scientific investigations, and these have been widely acclaimed by biologists. In fact, he has been inclined to overemphasize his supposed inadequacies with a frankness that he thought necessary for strict honesty. Most of the twenty-four chapters are written in narrative form and all of them with an unusual degree of literary excellence. They portray the development of the child into the mature man of science, with an analysis of the influences, hereditary and environmental, which may have guided this development along the course which was followed.

Of intense interest are the author's accounts of his early struggles in his chosen career, hampered as he

was by ill health, of his efforts to obtain definite proofs in his baffling scientific investigations, particularly those pertaining to natural selection and evolution, and of the persistence which eventually led to success. The narratives are enlivened by many amusing episodes and abound in clever and humorous expressions. The story of his ill-fated expedition to the Egyptian Sudan is as thrilling as almost any work of fiction.

As a general rule each chapter concludes with a brief discussion of the sociological aspects of the subject under consideration. The concluding chapters on the real value of science, man versus nature, the vivisection bogey and the philosophy of the booster are sound and forceful. The final comments on religious beliefs are the result of the author's honest conviction, although many will differ from his conclusions.

WESLEY R. COE

THE ASPERGILLI

Manual of the Aspergilli. By CHARLES THOM and KENNETH P. RAPER. 373 pp. Baltimore: Williams and Wilkins. 1945. $7.00.

THIS manual in general follows the plan or system of treatment found in a former work, "The *Aspergilli,*" by Thom and Church. While all the best features of that work have been preserved and added to in this book, it is in no sense merely a second edition or revision. It is an entirely new book written to include new knowledge acquired by the authors and others during the past twenty years. The subject-matter has been treated from a more modern viewpoint without abandoning such principles and conclusions as were strongly supported in the former work, and which have been found to be fundamentally sound.

It is gratifying to see that the authors have continued to maintain that the generic name *Aspergillus* should apply not only to the conidial stage but also to the ascosporic stage. The genus *Aspergillus* is here to stay, regardless of rules of nomenclature. "It is better," the authors say, "to forget *Eurotium* along with technicalities."

In Chapter 3, "Morphology and Description," as in the former work, the characters of the colony are discussed under such headings as (1) color, including the range of color extending through a group, color of conidial wall, chromogenesis or substratum coloration; (2) morphology of the head, foot-cells, stalk, vesicle, sterigmata and conidium formation. These features are more fully discussed and illustrated than formerly, so that a student understands what must first be known in order to identify a species correctly from the conidial stage alone. A comparatively small number of species develop ascocarps. These structures, including the "Hülle cells" and sclerotia, are briefly discussed. Sexual reproduction is strictly on the basis of homothallism. No heterothallic species are known so that variation as it occurs in nature and in culture can not be attributed to +/− relations. A variant is in general applied here to a strain which is not stable. It has arisen through gradual change from a well-defined strain. A mutant, on the other hand, they define as a strain whose source is known and has arisen from sharp breaks in culture. It is a gene mutation, and one which retains its distinguishing features in culture. Examples of natural and induced mutants are cited, though the authors do not pretend to distinguish absolutely an induced mutant from an induced variation.

Aspergillus has long been one of the classics for purposes of text-book illustration of the life history of an ascomycete. The authors could have, without detracting from the usefulness of the book, included more extended discussion of sexual reproduction along with illustrations of cytological features showing nuclear conditions in various structures and nuclear behavior leading up to ascus formation. The importance of heterocaryosis in the fungi is coming to be recognized so that a more extended discussion of this feature along with its many implications as determining colony characteristics would have been welcomed.

Chapter 4 on cultivation and examination has been considerably extended, now covering eighteen pages instead of eight. Nine excellent formulae are now recommended for culturing *Aspergillus.* Only one formula of the four originally suggested is retained. This is Czapek's Solution Agar. The special virtues of each type of medium are indicated. The pros and cons of "single spore" method of culture are interesting and instructive. The method has its place, but it can not be recommended as a way of preserving the whole morphology of a species. Transfer of masses of conidia is the best safeguard for this purpose. To this statement one could agree without giving up the idea that perhaps even then the whole morphology of a species would be difficult to corral in one culture. We are hearing much these days about the best way to maintain cultures of *Penicillium notatum* so as to insure the maximum production of penicillin.

The taxonomy of both of these genera demands the exercise of the most scrupulous care to preserve the purity of cultures. Chapter 5 on this subject has been enlarged to cover this subject more completely. The lyophile form of preservation of cultures for future use is described in some detail, but the authors point out that, while the feasibility of this method has not been fully proved, their results are encouraging. Various common sources of contamination are

again discussed and a good formula for poisoning cotton plugs against mite invasion has been added.

In Part II, the Manual Proper, the principle of bringing closely related forms together in "species groups," formerly strongly advocated because of the extreme variability of the species, has been further extended so that now the authors propose fourteen well-marked species groups. Three separate group keys enable even the non-expert to locate his species in the proper group, and this is about all most of us need. The authors accept only about ninety species, varieties and mutations; of these a dozen or so are mutations or varieties of good species.

Few of us have realized how easily one can locate a species by using a dichotomous diagram (Fig. 20): sterigmata present, absent; conidiophores smooth, rough; sclerotia present, absent; Hülle cells or not; conidiophore walls, smooth, rough. Group keys based (1) primarily on color and (2) on morphology cover the same ground.

Having determined to which of the fourteen species groups one's specimen belongs he turns to the special chapter on that group where additional keys subdivide that group into series. For example, the *A. glaucus* group is made up of nine species series. The *A. repens* series of this group consists of three distinct species. If a mycologist has studied his material properly in culture so that he really knows its morphology and culture characters he will have little trouble in identifying his species.

In the Manual Proper one finds morphological features all well figured. It would be difficult to find anywhere in the whole field of mycology more beautifully drawn figures of ascospores found in their figures 27, 34 and 43 where ascospores are figured from various angles. In addition to the inclusion of many half-tone and black and white illustrations, there are eight plates of photographs in color.

An extensive topical bibliography comprises Chapter 22. Literature on acid, enzyme and fat production, pathogenicity, physiology, pigments, soil tests, variation, growth substances, antibiotics, etc., is brought together topically. Reference to pages in the book where a number of these topics are discussed in the text will be found in the comprehensive index.

The "check list of genera and species" (Chapter 24) forms a very valuable part of the book. Sixteen generic names which have been applied to *Aspergillus* and some 600 species and variety names are covered briefly. Here all forms found in the literature are enumerated and their proper allocation is given in a way that serves as a guide to one who wishes to use the literature in the interpretation of names he finds but are "not known to him in nature, in cultures or in exsciti." The book brings *Aspergillus* up to date. It is one we must all possess, especially if we are interested in either *Aspergillus* or *Penicillium*.

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THE CALENDAR

Consider the Calendar. By BHOLA D. PANTH. New York: Bureau of Publications, Teachers College, Columbia University. 1944. $1.25.

USUALLY it is the chapter on "Time and the Calendar" in an astronomical text-book through which a college science student gets his first serious introduction to the problem of chronology and the relation of astronomical events to the clock on the mantelpiece and the calendar on the kitchen door. And most attempts to stimulate the interest of the student in calendar development and the need for calendar reform are distinctly inadequate—the subject of the calendar just seems to most students and laymen to be dull. Brief paragraphs, crammed full of cycles and epochs and eras, necessary in such aforementioned astronomy texts, do not improve the situation.

Therefore, supplementary reading is here especially important, and "Consider the Calendar" is just right for the purpose. It is the right length, too, and the student who reads it will not tend to skip important parts, because he knows its conclusion is on the 121st page. After he gets there, he will probably find himself reading Appendix A about holidays, and perhaps figuring out how to determine the day of the week using Appendix B. His interest will be stimulated enough by Mr. Panth's presentation to make him want to go out and spread his command of the calendar among his fellow students.

In Appendix C, Mr. Panth lists numerous books on the calendar. The trouble with most of them is that they are too specific, too lengthy, too boring, too repetitive—Mr. Panth has digested the salient facts of the problem and included in his well-written pages almost every calendar item of interest to the modern mind, scientific or otherwise.

We are told that the book is the outcome of a fellowship established by Teachers College for the study of the calendar from earliest times to our present day, including arguments for the adoption of a revised calendar more adequate for our daily use. His coverage of these points is in four main parts: the calendar in perspective; basic calendar concepts; basic calendar patterns; proposals and trends in calendar improvement.

Early in the book, Mr. Panth appraises the reader of his forthcoming attitude toward the Gregorian calendar: "It is a lingering medieval instrument operating in a highly advanced and synchronized technological society." Throughout, he never misses a chance to point out the inadequacy of the 28 dif-

ferent kinds of months possible in the present system. He brings to this reviewer's mind the full impact of the calendar's lack of respect for the schedules of a monthly publication—the wearing effect on printer, author, editor, publisher, of deadlines by date occurring at all sorts of times in the week, and the deleterious effect of holidays sprinkled here and there in the work routine. Mr. Panth's description of the extra effort spent by our 248,000 schools, colleges and universities in the continental United States as they plan their programs each year is truly impressive; the far-reaching effect these school plans have on a host of other institutions and industries can provoke any reader into realizing that in his case, too, the calendar is helping him to waste some of his life.

The two outstanding plans for calendar reform, 12-month equal quarters and 13-month calendars, are fully discussed, including facts to the effect that by 1938 fourteen governments of the world had approved the World Calendar; six opposed it; and twenty-five were on the fence or otherwise not interested. The United States had "no observations to submit," which is an attitude we hope will change to definite positive action as soon as the United Nations consider social and economic reforms of international significance—the calendar problem can well be placed near the top of the list of important international reforms. On this score, Mr. Panth is optimistic, believing that World War II will help the calendar to follow the example of standard time in becoming internationalized.

Easter comes in for its usual share of the discussion. It seems to the writer that this is not really a problem for the calendar, but for civil and religious authorities—the shifting dates of Easter can be eliminated simply and quickly, or at least confined to whatever date falls on the second Sunday in April, a plan already adopted in England. Mr. Panth errs slightly in repeatedly defining Easter as falling on the Sunday following the first full moon after the vernal equinox. He should refer to the fourteenth day of the moon and to March 21st, and should also mention that the "moon" used is a calendric one having only a vague similarity to the one in the sky in the matter of dates for phase occurrences.

Elsewhere, in describing basic calendar concepts, Mr. Panth says the earth revolves around the sun in a *tropical* year, and on page 32 he says the moon makes one complete circuit of the earth in 29.530588 days, or one *synodic* month. Later he correctly describes the month of the moon's revolution as *sidereal*, 27⅓ days long, but nowhere does he correctly define the earth's *sidereal* year and point out the difference in its length compared with the tropical year. He might have had an interesting point by noting that a person celebrating an age of 72 calendar years must really wait one more full day to complete 72 trips around the sun. Also, it is notable that there is no mention of the precessional cycle of 25,800 years.

On page 85, item 4 points out that the two halves of the year are unequal in our present calendar; in common years they are 181 and 184 days long. Previously, item 1 on page 84 criticizes the calendar for not beginning at a solstice or an equinox, a "natural division" for marking time. If such a beginning is desirable and is to be combined with equal halves, calendar makers are doomed partly to disappointment, for the earth's variable revolution gives us quite unequal halves as measured from equinox to equinox; 179 days for fall and winter, and 186 days for spring and summer, in the Northern Hemisphere.

Except for this, however, Mr. Panth's lists of pros and cons on calendar reform are very complete and scholarly and sensible. His numerous charts furnish ample opportunity for one to verify his arguments and make additional comparisons of all kinds of calendars. The histories and operating details of Jewish, Roman, Mohammedan and other calendars are adequately presented, as well as facts concerning the calendars of the French revolutionists, the Soviet republics, and of some of the 185 plans from 33 countries submitted to the League of Nations in 1926. It may be surprising to know that in 1942 over a thousand commercial concerns in the United States and Canada were using internally a 13-period work calendar, consisting mainly of 13 months of four weeks each. It is significant, then, that United States Civil Service this August replaced semi-monthly with bi-weekly payroll periods.

It seems inevitable that our "medieval" calendar will eventually be replaced. "Consider the calendar" is good advice to scientists in general and teachers in particular, for by educating the public to take a scientific attitude toward this problem the chief obstacles, government inertia and religious scruples, will be overcome.

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